

	L #	Hits	Search Text	DBs	Time Stamp
1	L1	1660	424/130.1,133.1,134.1,135.1,136.1,138.1,141.1,142.1,143.1,152.1,155.1,156.1172.1,173.1,174.1.ccls.	USPA T	2002/10/25 15:08
2	L2	1401	egfr or errbl or cerbb1 or (epidermal adj growth adj factor adj receptor)	USPA T	2002/10/25 15:08
3	L3	85	1 and 2	USPA T	2002/10/25 14:52
4	L4	407	424/130.1,133.1,134.1,135.1,136.1,138.1,141.1,142.1,143.1,152.1,155.1,156.1172.1,173.1,174.1.ccls.	US-P GPUB	2002/10/25 15:08
5	L5	410	egfr or errbl or cerbb1 or (epidermal adj growth adj factor adj receptor)	US-P GPUB	2002/10/25 15:08
6	L6	33	4 and 5	US-P GPUB	2002/10/25 15:08

10-25-02

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L40 ANSWER 1 OF 76 MEDLINE
ACCESSION NUMBER: 2002113263 MEDLINE
DOCUMENT NUMBER: 21834363 PubMed ID: 11845796
TITLE: ImClone BLA is declined.
COMMENT: Comment in: Nat Biotechnol. 2002 Feb;20(2):101
Comment in: Nat Biotechnol. 2002 Feb;20(2):101
AUTHOR: Fletcher Liz
SOURCE: NATURE BIOTECHNOLOGY, (2002 Feb) 20 (2) 111.
Journal code: 9604648. ISSN: 1087-0156.
PUB. COUNTRY: United States
DOCUMENT TYPE: News Announcement
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200205
ENTRY DATE: Entered STN: 20020216
Last Updated on STN: 20020507
Entered Medline: 20020506

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cancer res.
53: 4327-4328
1993*

L40 ANSWER 2 OF 76 MEDLINE
ACCESSION NUMBER: 2002368496 MEDLINE
DOCUMENT NUMBER: 22108440 PubMed ID: 12113039
TITLE: ERBITUX as a single agent and in combination in
colorectal carcinoma.
AUTHOR: Anonymous
SOURCE: Expert Rev Anticancer Ther, (2002 Jun) 2 (3) 242.
Journal code: 101123358. ISSN: 1473-7140.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: News Announcement
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200208
ENTRY DATE: Entered STN: 20020713
Last Updated on STN: 20020816
Entered Medline: 20020815

L40 ANSWER 3 OF 76 MEDLINE
ACCESSION NUMBER: 2002110841 MEDLINE
DOCUMENT NUMBER: 21679656 PubMed ID: 11821837
TITLE: Nothing succeeds like failure.
COMMENT: Comment on: Nat Biotechnol. 2002 Feb;20(2):111
AUTHOR: Anonymous
SOURCE: NATURE BIOTECHNOLOGY, (2002 Feb) 20 (2) 101.
Journal code: 9604648. ISSN: 1087-0156.
PUB. COUNTRY: United States
DOCUMENT TYPE: Commentary
Editorial
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200205
ENTRY DATE: Entered STN: 20020215
Last Updated on STN: 20020507
Entered Medline: 20020506

L40 ANSWER 4 OF 76 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:716015 CAPLUS
DOCUMENT NUMBER: 137:226593
TITLE: Method for ***treating*** cancer using A33
specific antibodies and chemotherapeutic agents
INVENTOR(S): Welt, Sydney; Kemeny, Nancy; Ritter, Gerd; Jungbluth,
Achim A.; Old, Lloyd J.; Cohen, Leonard
PATENT ASSIGNEE(S): Ludwig Institute for Cancer Research, USA; Sloan
Kettering Institute for Cancer Research
SOURCE: PCT Int. Appl., 54 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002072008	A2	20020919	WO 2002-US6902	20020308

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2001-800522 A 20010308

AB This invention relates to a combination of immunotherapy and chemotherapy to promote tumor regression by ***treating*** a patient in need thereof with a combination of an antibody that binds to A33 antigen and one or more chemotherapeutic agents. The method is useful for ***treating*** patients with ***colorectal*** cancer and gastric carcinomas. The method is particularly useful for ***treating*** patients who have tumors that are resistant to one or more chemotherapeutic agents and/or have metastasized.

L40 ANSWER 5 OF 76 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.

ACCESSION NUMBER: 2002096723 EMBASE

TITLE: ***Monoclonal*** antibodies to target epidermal growth factor receptor-positive tumors a new paradigm for cancer therapy.

AUTHOR: Herbst R.S.; Shin D.M.

CORPORATE SOURCE: Dr. R.S. Herbst, Dept. Thorac. Head/Neck Med. Oncol., M. D. Anderson Cancer Center, Box 432, 1515 Holcombe Boulevard, Houston, TX 77030-4009, United States.
rherbst@mdanderson.org

SOURCE: Cancer, (1 Mar 2002) 94/5 (1593-1611).

Refs: 149

ISSN: 0008-543X CODEN: CANCAR

COUNTRY: United States

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 014 Radiology

016 Cancer

026 Immunology, Serology and Transplantation

037 Drug Literature Index

038 Adverse Reactions Titles

LANGUAGE: English

SUMMARY LANGUAGE: English

AB BACKGROUND. Traditional cytotoxic approaches to tumor management are associated with efficacy and toxicity limitations. Blockade of the epidermal growth factor receptor (***EGFR***) and its ligands is a novel approach to the treatment of human tumors that offers a noncytotoxic alternative to cancer treatment. METHODS. An English-language literature search was conducted to identify studies assessing the in vitro and in vivo effects of ***EGFR*** blockade with an emphasis on approaches that use ***monoclonal*** antibody therapy. RESULTS. The EGF pathway regulates normal cellular processes and appears to be correlated with the development of malignancy. Approximately 30% of human tumors express ***EGFR*** , which has been reported to be correlated with poor prognosis and diminished disease-free and overall survival in selected tumor types. A number of anti- ***EGFR*** ***monoclonal*** antibodies have been developed, which currently are undergoing clinical trials in humans. Effective anti- ***EGFR*** ***monoclonal*** antibodies compete with endogenous ligands, primarily EGF and transforming growth factor- α , for receptor ligand-binding sites. Binding to ***EGFR*** blocks critical signaling pathways and interferes with the growth of tumors expressing ***EGFR*** . Anti- ***EGFR*** ***monoclonal*** antibodies that currently are under study include IMC-C225, EMD 55900, ICR

62, and ABX-EGF. CONCLUSIONS. These antibodies have demonstrated promising results and appear to have been well tolerated. ***EGFR*** -targeted therapy addresses important, unmet needs in the treatment of human tumors, particularly ***EGFR*** -positive epithelial tumors including common malignancies of the head and neck, lung, and colon. .COPYRG. 2002 American Cancer Society.

L40 ANSWER 6 OF 76 MEDLINE
 ACCESSION NUMBER: 2002430001 IN-PROCESS
 DOCUMENT NUMBER: 22173579 PubMed ID: 12186273
 TITLE: Cetuximab (Imclone/Merck/Bristol-Myers Squibb).
 AUTHOR: Kies Merrill S; Harari Paul M
 CORPORATE SOURCE: University of Texas MD Anderson Cancer Center, Houston
 77030, USA.. mkies@mail.mdanderson.org
 SOURCE: Curr Opin Investig Drugs, (2002 Jul) 3 (7) 1092-100.
 Journal code: 100965718. ISSN: 1472-4472.
 PUB. COUNTRY: England: United Kingdom
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 LANGUAGE: English
 FILE SEGMENT: IN-PROCESS; NONINDEXED; Priority Journals
 ENTRY DATE: Entered STN: 20020821
 Last Updated on STN: 20020821

AB ImClone, in collaboration with licensees, Merck KGaA and Bristol-Myers Squibb (BMS), are developing cetuximab, a ***chimeric***
 monoclonal antibody that blocks the epidermal growth factor receptor, for the potential ***treatment*** of various cancers, including ***colorectal***, and head and neck tumors [179103]. The companies are evaluating the product both as a single agent, and in combination with radiation and a variety of chemotherapeutic agents. By January 2002, phase III trials had been initiated in head and neck cancer, and phase II trials were ongoing for ***colorectal*** and other cancers [427710], [437833]. In November 2001, ImClone completed the filing of a rolling BLA with the FDA for cetuximab in combination with ***irinotecan*** to ***treat*** ***irinotecan*** -refractory ***colorectal*** cancer. In December 2001, however, the FDA advised ImClone that its BLA was not acceptable for filing. In January 2002, it was reported that resubmission of the BLA was expected within 3 months [434999], and by February 2002, ImClone was expecting to use data from an ongoing phase II study in ***colorectal*** cancer patients conducted by Merck KGaA. In March 2002, Merck had anticipated European launch in 2003 [444653]; however, in April 2002, Merck reported that it was delaying its application to the European Agency for the Evaluation of Medicinal Products from the last half of 2002 to the first half of 2003, so that it could primarily include its own ***colorectal*** cancer data rather than ImClone's data. European launch was thus expected in 2004 [449226]. In May 2002, Lehman Brothers predicted global peak sales of US \$2 billion [454652], while in the same month, Bear Stearns estimated that sales for Merck KGaA would reach 285 million Euros in 2007 [453500].

L40 ANSWER 7 OF 76 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
 ACCESSION NUMBER: 2002154900 EMBASE
 TITLE: Systemic ***treatment*** of ***colorectal*** cancer.
 AUTHOR: Tebbutt N.C.; Cattell E.; Midgley R.; Cunningham D.; Kerr D.
 CORPORATE SOURCE: N.C. Tebbutt, Department of Medicine, Royal Marsden Hospital, Downs Road, Sutton Surrey, SM2 5PT, United Kingdom. niall.tebbutt@rmh.nthames.nhs.uk
 SOURCE: European Journal of Cancer, (2002) 38/7 (1000-1015).
 Refs: 91
 ISSN: 0959-8049 CODEN: EJCAEL
 PUBLISHER IDENT.: S 0959-8049(02)00062-X
 COUNTRY: United Kingdom
 DOCUMENT TYPE: Journal; Article
 FILE SEGMENT: 016 Cancer
 037 Drug Literature Index
 038 Adverse Reactions Titles

048 Gastroenterology

LANGUAGE: English

SUMMARY LANGUAGE: English

AB Palliative and adjuvant ***treatment*** for ***colorectal*** cancer has been, until recently, largely dependent on 5-fluorouracil (5-FU)-based chemotherapy. Oral fluoropyrimidines have been evaluated in the advanced disease setting and they appear to be as effective as 5-FU, but are safer and more convenient for most patients. ***Irinotecan*** and oxaliplatin are new cytotoxic agents, which are active in 5-FU-resistant disease, but which may also be combined with 5-FU as initial ***therapy*** in advanced disease. Initial combination ***therapy*** leads to improved response rates and more prolonged progression-free survival compared with 5-FU monotherapy. Standard regimens for adjuvant ***therapy*** usually involve 6 months of chemotherapy using 5-FU and folinic acid. Recent trials of capecitabine, oxaliplatin and ***irinotecan*** in the adjuvant setting are ongoing, or have recently completed accrual, and may lead to a change in future clinical practice. Biological ***therapies*** are playing an increasing role in the management of ***colorectal*** cancer. Farnesyl transferase inhibition, inhibition of the epidermal growth factor receptor (***EGFR***) and the vascular endothelial growth factor (VEGF) are undergoing evaluation in advanced disease. In the adjuvant setting, both passive and active immunotherapeutic approaches have been studied. In addition, a large trial will evaluate the role of cyclo-oxygenase(COX)-2 inhibitors as adjuvant ***therapy***. Further research is required in order to define the optimal sequence and combination of these different cytotoxic and biological ***therapies***, in order to secure the best possible outcome for various subgroups of patients with both early and advanced stage ***colorectal*** cancer. .COPYRG.T. 2002 Published by Elsevier Science Ltd.

L40 ANSWER 8 OF 76 MEDLINE

ACCESSION NUMBER: 2002266675 MEDLINE

DOCUMENT NUMBER: 22000989 PubMed ID: 12006511

TITLE: Enhanced antitumor activity of anti-epidermal growth factor receptor ***monoclonal*** antibody IMC-C225 in combination with ***irinotecan*** (CPT-11) against human ***colorectal*** tumor xenografts.

AUTHOR: Prewett Marie C; Hooper Andrea T; Bassi Rajiv; Ellis Lee M; Waksal Harlan W; Hicklin Daniel J

CORPORATE SOURCE: Department of Immunology, ImClone Systems, Inc., New York, New York 10014, USA.

SOURCE: CLINICAL CANCER RESEARCH, (2002 May) 8 (5) 994-1003.
Journal code: 9502500. ISSN: 1078-0432.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200210

ENTRY DATE: Entered STN: 20020514

Last Updated on STN: 20021018

Entered Medline: 20021017

AB Colon carcinomas frequently express the epidermal growth factor receptor (***EGFR***), and this expression correlates with more aggressive disease and poor prognosis. Previous studies have shown that ***EGFR*** blockade by ***monoclonal*** antibody IMC-C225 can inhibit the growth of human colon carcinoma tumor cells in vitro and xenografts of these tumors in athymic mice. In this report, we have studied the in vivo activity of IMC-C225 combined with the topoisomerase I inhibitor ***irinotecan*** (CPT-11) using two models of human ***colorectal*** carcinoma in nude mice. IMC-C225 was tested at a dose of 1 or 0.5 mg administered q3d. CPT-11 was administered at a dose of 100 mg/kg/week or a maximum tolerated dose of 150 mg/kg/week. ***Treatment*** with the combination of IMC-C225 (1 and 0.5 mg) and CPT-11 (100 mg/kg) significantly inhibited the growth of established DLD-1 and HT-29 tumors compared with either CPT-11 or IMC-C225 monotherapy ($P < 0.05$). Combination ***therapy*** with IMC-C225 (1 mg) and the MTD of CPT-11

(150 mg/kg) resulted in a regression rate of 100 and 60% of established DLD-1 and HT-29 tumors, respectively. In a refractory tumor model, combined ***treatment*** with IMC-C225 and CPT-11 significantly inhibited the growth of CPT-11 refractory DLD-1 and HT-29 tumors, whereas either agent alone did not control tumor growth. Histological examination of ***treated*** tumors showed extensive tumor necrosis, decreased tumor cell proliferation, increased tumor cell apoptosis, and a marked decrease in tumor vasculature. These results suggest that ***EGFR*** blockade by IMC-C225 combined with topoisomerase I inhibitors may be an effective ***therapy*** against chemorefractory ***colorectal*** carcinoma tumors.

L40 ANSWER 9 OF 76 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.

ACCESSION NUMBER: 2002206862 EMBASE

TITLE: Recent and ongoing clinical trials for ***treating***
colorectal cancer.

AUTHOR: Mulcahy M.F.; Benson III A.B.

CORPORATE SOURCE: Dr. A.B. Benson III, Northwestern University, Division of Hematology and Oncology, Department of Medicine, 676 North Saint Clair, Chicago, IL 60611, United States.
a-benson@northwestern.edu

SOURCE: Expert Opinion on Investigational Drugs, (2002) 11/6 (871-880).

Refs: 85

ISSN: 1354-3784 CODEN: EOIDER

COUNTRY: United Kingdom

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 016 Cancer

030 Pharmacology

037 Drug Literature Index

038 Adverse Reactions Titles

048 Gastroenterology

LANGUAGE: English

SUMMARY LANGUAGE: English

AB ***Colorectal*** cancer is one of the most common cancers worldwide.

Through well-designed clinical trials, advances have been made in the ***treatment*** of localised and advanced ***colorectal*** cancer. It has been established that 6 months of 5-fluorouracil-based chemotherapy will improve overall survival in patients with stage III colon cancer. The role of adjuvant chemotherapy in stage II colon cancer remains an unresolved issue. Recent studies have demonstrated an improved survival with the addition of ***irinotecan*** to 5-fluorouracil and leucovorin for the ***treatment*** of advanced ***colorectal*** cancer. Immunotherapy, molecular targeted ***therapy*** and liver-directed ***therapy***, in addition to new chemotherapy combinations, are all being evaluated for the ***treatment*** of localised and advanced ***colorectal*** cancer. Ongoing and proposed studies are incorporating the identification of genetic and molecular abnormalities, which may provide prognostic information as well as direct ***treatment*** decisions.

L40 ANSWER 10 OF 76 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: 2002:409154 BIOSIS

DOCUMENT NUMBER: PREV200200409154

TITLE: Enhanced antitumor activity of anti-epidermal growth factor receptor ***monoclonal*** antibody ERBITUXTM (IMC-C225) in combination with ***irinotecan*** (CPT-11), 5-FU, and leucovorin against human ***colorectal*** carcinoma xenografts.

AUTHOR(S): Prewett, Marie C. (1); Hooper, Andrea T. (1); Bassi, Rajiv (1); Waksal, Harlan W. (1); Hicklin, Daniel J. (1)

CORPORATE SOURCE: (1) ImClone Systems Incorporated, New York, NY USA

SOURCE: Proceedings of the American Association for Cancer Research Annual Meeting, (March, 2002) Vol. 43, pp. 581. print.
Meeting Info.: 93rd Annual Meeting of the American Association for Cancer Research San Francisco, California, USA April 06-10, 2002

ISSN: 0197-016X.
DOCUMENT TYPE: Conference
LANGUAGE: English

L40 ANSWER 11 OF 76 MEDLINE
ACCESSION NUMBER: 2002174022 MEDLINE
DOCUMENT NUMBER: 21903031 PubMed ID: 11904970
TITLE: Clinical assessment of ***monoclonal*** antibodies for
the ***treatment*** and diagnosis of ***colorectal***
cancers.
AUTHOR: Koda Keiji; Miyazaki Masaru
CORPORATE SOURCE: Department of General Surgery, Graduate School of Medicine,
Chiba University.
SOURCE: NIPPON RINSHO. JAPANESE JOURNAL OF CLINICAL MEDICINE, (2002
Mar) 60 (3) 539-44. Ref: 19
Journal code: 0420546. ISSN: 0047-1852.
PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: Japanese
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200204
ENTRY DATE: Entered STN: 20020322
Last Updated on STN: 20020410
Entered Medline: 20020409

AB The clinically useful ***monoclonal*** antibodies(Mabs) for
colorectal cancers were reviewed. Since 1980's, immunoscintigraphy
has been performed for the detection of occult ***colorectal***
cancers. However, it may be substituted with the development of positron
emission tomography. As for the ***treatment***, some Mabs have been
shown to be effective for the adjuvant ***therapy*** of postoperative
colorectal cancers. Some Mabs to epidermal growth factor
receptors(***EGFr***) are quite promising since they block the
functions necessary for the tumor growth and enhance the cytotoxicity of
chemotherapy. Recent advances for the development of ***humanized***
Mabs will improve the chance of Mabs to be used as an effective adjuvant.

L40 ANSWER 12 OF 76 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2002:408715 BIOSIS
DOCUMENT NUMBER: PREV200200408715
TITLE: Phase I trial of the ***humanized*** anti epidermal
growth factor receptor (***EGFr***) ***monoclonal***
antibody EMD 72000 in patients (pts) with ***EGFr***
expressing solid tumors.
AUTHOR(S): Tewes, Mitra (1); Schleucher, Norbert; Dirsch, Olaf;
Schmid, Kurt Werner; Arens, Hans-Juergen; Seeber,
Siegfried; Harstrick, Andreas; Vanhoefer, Udo
CORPORATE SOURCE: (1) Dept. of Internal Medicine, West German Cancer Center,
Essen Germany
SOURCE: Proceedings of the American Association for Cancer Research
Annual Meeting, (March, 2002) Vol. 43, pp. 490-491. print.
Meeting Info.: 93rd Annual Meeting of the American
Association for Cancer Research San Francisco, California,
USA April 06-10, 2002
ISSN: 0197-016X.
DOCUMENT TYPE: Conference
LANGUAGE: English

L40 ANSWER 13 OF 76 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 2002277464 MEDLINE
DOCUMENT NUMBER: 22012751 PubMed ID: 12018689
TITLE: Current concepts in immunotherapy for the ***treatment***
of ***colorectal*** cancer.
AUTHOR: Indar A; Maxwell-Armstrong C A; Durrant L G; Carmichael J;
Scholefield J H
CORPORATE SOURCE: Division of Surgery, Queens Medical Centre, Nottingham,

UK.. Adrian.Indar@nottingham.ac.uk
 SOURCE: JOURNAL OF THE ROYAL COLLEGE OF SURGEONS OF EDINBURGH,
 (2002 Apr) 47 (2) 458-74. Ref: 147
 Journal code: 7503110. ISSN: 0035-8835.
 PUB. COUNTRY: Scotland: United Kingdom
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 General Review; (REVIEW)
 (REVIEW, ACADEMIC)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 200206
 ENTRY DATE: Entered STN: 20020522
 Last Updated on STN: 20020619
 Entered Medline: 20020618

AB Immunotherapy could have a role in the ***therapy*** of
 colorectal cancer as there is now convincing evidence that the
 immune system can specifically recognize and destroy malignant cells. The
 MAb 17-1A has been used in advanced and primary disease, along
 with newer agents such as anti-epidermal growth factor receptor (
 EGFR) antibody. Immunotherapy with autologous tumour cell vaccine,
 genetic modification of immunostimulatory cytokines, suicide genes and
 TAAs as discussed. The multiplicity of peptide and carbohydrate antigens
 which can be potential targets for immunotherapy are also discussed. These
 include MUC1, Thomsen-Friedenreich and Sialosyl-Tn antigens and HER2 /
 neu. Active specific immunotherapy with the anti-idiotypic antibodies
 CEAVac and 105AD7, along with DC vaccines, is being currently used in
 adjuvant clinical trials. 105AD7 has been shown to cause significantly
 greater apoptosis of tumour cells in ***colorectal*** cancer patients,
 while CEAVac generated T cell proliferative anti-CEA responses. Dendritic
 cells pulsed with tumour mRNA or TAAs currently are being assessed in
 clinical trials. The role of HSPs in the anti-tumour immune response is
 discussed. Non-specific immunotherapeutic agents used in clinical trials
 with chemotherapeutic regimens have not shown any definitive benefit.
 Tumour progression may occur as result of escape from the host anti-cancer
 immune response. Better understanding of mechanisms of tumour evasion
 could explain why immunotherapy trials in patients have not shown better
 results. These include down-regulation of immune responses by the tumour,
 altered expression of MHC and/or TAAs by tumour cells, altered expression
 of adhesion molecules by tumour and/or DCs and usurpation of the immune
 response to the advantage of the cancer.

L40 ANSWER 14 OF 76 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
 ACCESSION NUMBER: 2002207393 EMBASE
 TITLE: [Medical ***treatment*** of ***colorectal***
 cancer].
 DIE MEDIKAMENTÖSE ***THERAPIE*** DES KOLOREKTALEN
 KARZINOMS.
 AUTHOR: Ulrich-Pur H.; Jech B.; Scheithauer W.; Kornek G.V.; Huber
 H.
 CORPORATE SOURCE: Dr. H. Ulrich-Pur, Klinische Abteilung für Onkologie, Univ.
 Klin. für Innere Medizin I, Wahringer Gürtel 18-20, A-1090
 Wien, Austria. herbert.ulrich-pur@akh-wien.ac.at
 SOURCE: Wiener Klinische Wochenschrift, (14 Jun 2002) 114/10-11
 (368-376).
 Refs: 63
 ISSN: 0043-5325 CODEN: WKWOAO
 COUNTRY: Austria
 DOCUMENT TYPE: Journal; General Review
 FILE SEGMENT: 006 Internal Medicine
 016 Cancer
 037 Drug Literature Index
 LANGUAGE: German
 SUMMARY LANGUAGE: English; German

AB ***Colorectal*** cancer represents one of the most common malignant
 diseases worldwide. Because of the expanding understanding of the biology
 of this disease entity, and the development/availability of a number novel
 antitumor agents, ***therapeutic*** options have considerably improved

within the past few years. As for new drug development, ***therapeutic*** advances comprise the oral fluoropyrimidine prodrugs, specific thymidilate synthase inhibitors, ***irinotecan***, oxaliplatin, and signal transduction inhibitors such as the anti-EGF-receptor ***monoclonal*** antibody Cetuximab. Compared to the area of conventional 5-fluorouracil ***therapy***, much higher objective response rates and major improvements in overall survival can be achieved today, even in the case of disseminated disease. The aim of this review article is to provide the reader with an overview of presently available ***treatment*** options in the palliative, neoadjuvant and postoperative adjuvant setting in colon and rectal cancer, respectively. Furthermore, actual clinical-practice oriented and future perspectives in the management of this disease will be addressed.

L40 ANSWER 15 OF 76 MEDLINE

ACCESSION NUMBER: 2002173702 MEDLINE

DOCUMENT NUMBER: 21903047 PubMed ID: 11904986

TITLE: Molecular target-based cancer ***therapy*** : epidermal growth factor receptor inhibitors.

AUTHOR: Tamura Tomohide

CORPORATE SOURCE: Division of Internal Medicine, National Cancer Center Hospital, Tokyo, Japan.

SOURCE: NIPPON GEKA GAKKAI ZASSHI. JOURNAL OF JAPAN SURGICAL SOCIETY, (2002 Feb) 103 (2) 233-6. Ref: 10
Journal code: 0405405. ISSN: 0301-4894.

PUB. COUNTRY: Japan

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)

LANGUAGE: Japanese

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200204

ENTRY DATE: Entered STN: 20020322

Last Updated on STN: 20020424

Entered Medline: 20020423

AB Based on recent progress in cancer biology, numerous molecules that contribute to proliferation, invasion, and metastasis of cancer cells have been identified. The epidermal growth factor receptor (***EGFR***), a member of cell membrane receptors, is overexpressed by many tumors, and ***EGFR*** overexpression correlates with poor prognosis and disease progression. The ***EGFR*** is an attractive target for novel anticancer ***therapy***. ZD1839 and OSI-774, highly specific ***EGFR*** tyrosine kinase inhibitors, have shown promising antitumor activity against cisplatin-resistant non-small cell lung cancer in phase I and phase II trials. IMC-C225, a ***monoclonal*** antibody against ***EGFR***, has achieved significant disease control in head and neck cancer and ***colorectal*** cancer in combination with anticancer agents. These agents are under evaluation in phase III trials. In conclusion, it is expected that ***EGFR*** -directed ***therapies*** will soon be established as an effective novel ***treatment*** for many cancer patients.

L40 ANSWER 16 OF 76 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.

ACCESSION NUMBER: 2002069902 EMBASE

TITLE: Nothing succeeds like failure.

SOURCE: Nature Biotechnology, (2002) 20/2 (101).

ISSN: 1087-0156 CODEN: NABIF

COUNTRY: United States

DOCUMENT TYPE: Journal; Editorial

FILE SEGMENT: 016 Cancer

026 Immunology, Serology and Transplantation

036 Health Policy, Economics and Management

037 Drug Literature Index

039 Pharmacy

LANGUAGE: English

L40 ANSWER 17 OF 76 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: 2002:543333 BIOSIS
 DOCUMENT NUMBER: PREV200200543333
 TITLE: Phase 1 clinical trial of ABX-EGF, a fully human anti-epidermal growth factor receptor (***EGFR***) ***monoclonal*** antibody (***mAb***) for patients with advanced cancer.
 AUTHOR(S): Figlin, R. (1); Beldegrun, A.; Crawford, J.; Lohner, M.; Roskos, L.; Yang, X. D.; Foon, K. A.; Schwab, G.; Weiner, L.
 CORPORATE SOURCE: (1) Oncology, UCLA School of Medicine, Los Angeles, CA: gonzales_d@abgenix.com USA
 SOURCE: International Journal of Cancer Supplement, (2002) No. 13, pp. 87. print.
 Meeting Info.: 18th UICC International Cancer Congress
 Oslo, Norway June 30-July 05, 2002
 ISSN: 0898-6924.
 DOCUMENT TYPE: Conference
 LANGUAGE: English

L40 ANSWER 18 OF 76 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
 ACCESSION NUMBER: 2002349650 EMBASE
 TITLE: Highlights from: 38th Annual Meeting of the American Society of Clinical Oncology. Edrecolomab (Panorex.RTM.) in combination with 5-fluorouracil-Based Adjuvant chemotherapy in stage III colon cancer.
 SOURCE: Clinical Colorectal Cancer, (2002) 2/2 (73-77).
 Refs: 27
 ISSN: 1533-0028 CODEN: CCCLCF
 COUNTRY: United States
 DOCUMENT TYPE: Journal; Conference Article
 FILE SEGMENT: 016 Cancer
 030 Pharmacology
 037 Drug Literature Index
 038 Adverse Reactions Titles
 048 Gastroenterology
 LANGUAGE: English

L40 ANSWER 19 OF 76 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
 ACCESSION NUMBER: 2002226995 EMBASE
 TITLE: Thymidylate synthase expression as a predictor of clinical response to fluoropyrimidine-based chemotherapy in advanced ***colorectal*** cancer.
 AUTHOR: Aschele C.; Lonardi S.; Monfardini S.
 CORPORATE SOURCE: Dr. C. Aschele, Divisione di Oncologia Medica, Azienda Ospedaliera di Padova, via Giustiniani 2, 35128 Padova, Italy. aschele@tin.it
 SOURCE: Cancer Treatment Reviews, (2002) 28/1 (27-47).
 Refs: 131
 ISSN: 0305-7372 CODEN: CTREDJ
 COUNTRY: United Kingdom
 DOCUMENT TYPE: Journal; General Review
 FILE SEGMENT: 016 Cancer
 029 Clinical Biochemistry
 030 Pharmacology
 037 Drug Literature Index
 048 Gastroenterology
 LANGUAGE: English
 SUMMARY LANGUAGE: English

AB Thymidylate Synthase (TS) is a rate-limiting enzyme in the DNA synthetic pathway and represents the cellular target of the antimetabolite drug 5-fluorouracil (FUra). Both preclinical and clinical studies have shown that the level of expression of this enzyme and the ability to achieve its inhibition are the major determinants of sensitivity and resistance to fluoropyrimidines (FP). In particular, five recent studies have consistently demonstrated an inverse correlation between the level of TS gene or protein expression measured in ***colorectal*** cancer metastases and the clinical response to either FUra or

5-fluorodeoxyuridine (FUdR). Patients with low levels of TS expression in their metastases have indeed shown response rates that are three to ten times higher compared to those obtained in patients with high TS levels. The independent predictive value demonstrated in a logistic regression model, the longer survival shown by patients with low TS levels in three of five studies and the consistency of the results obtained by independent groups using different techniques to quantitate TS expression, strengthen the predictive role of TS. Targeted ***treatment*** of ***colorectal*** cancer based on TS quantitation has thus been hypothesized similar to the use of hormone receptor in breast cancer. In this review preclinical and clinical data supporting the use of TS quantitation to predict for the clinical response to FUra will be described and unresolved problems including assays standardization, response prediction based on TS levels measured in primary tumors, inpatient variations in TS levels and biological/biochemical limitations of this strategy will be discussed. .COPYRG. 2002, Elsevier Science Ltd. All rights reserved.

L40 ANSWER 20 OF 76 MEDLINE
 ACCESSION NUMBER: 2002311759 MEDLINE
 DOCUMENT NUMBER: 22049733 PubMed ID: 12053861
 TITLE: The role of the epidermal growth factor receptor in the
 treatment of ***colorectal*** carcinoma.
 AUTHOR: Waxman Elizabeth S; Herbst Roy S
 CORPORATE SOURCE: Department of Thoracic Medical Oncology, M. D. Anderson
 Cancer Center, University of Texas, Houston, USA.
 SOURCE: SEMINARS IN ONCOLOGY NURSING, (2002 May) 18 (2 Suppl 2)
 20-9. Ref: 54
 Journal code: 8504688. ISSN: 0749-2081.
 PUB. COUNTRY: United States
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 General Review; (REVIEW)
 (REVIEW, TUTORIAL)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals; Nursing Journals
 ENTRY MONTH: 200208
 ENTRY DATE: Entered STN: 20020611
 Last Updated on STN: 20020823
 Entered Medline: 20020822
 AB OBJECTIVES: To review the implications of epidermal growth factor receptor
 (***EGFR***) blockade and become familiar with the clinical experience
 in ***colorectal*** carcinoma to date. DATA SOURCES: Research articles
 and textbooks. CONCLUSIONS: Blockade of the ***EGFR*** results in
 clinically significant antitumor activities in a variety of tumors,
 including ***colorectal*** carcinoma. There are a variety of
 mechanisms by which to block the ***EGFR*** pathway. Those that have
 undergone extensive clinical testing include tyrosine kinase inhibitors
 and anti- ***EGFR*** ***monoclonal*** antibodies. In addition,
 biological agents have shown promise when combined with traditional
 cytotoxic approaches. IMPLICATIONS FOR NURSING PRACTICE: With many
 targeted biological agents undergoing evaluation, it is important that
 nurses become familiar with early clinical experience to understand their
 role in the ***treatment*** of cancer.

L40 ANSWER 21 OF 76 MEDLINE
 ACCESSION NUMBER: 2002442072 IN-PROCESS
 DOCUMENT NUMBER: 22187612 PubMed ID: 12199627
 TITLE: Targeting vascular endothelial growth factor in
 colorectal cancer.
 AUTHOR: Berlin Jordan D
 CORPORATE SOURCE: Vanderbilt Medical Center, Nashville, Tennessee, USA..
 jordan.berlin@mcm.vanderbilt.edu
 SOURCE: ONCOLOGY, (2002 Aug) 16 (8 Suppl 7) 13-5.
 Journal code: 8712059. ISSN: 0890-9091.
 PUB. COUNTRY: United States
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 LANGUAGE: English

FILE SEGMENT: IN-PROCESS; NONINDEXED; Priority Journals

ENTRY DATE: Entered STN: 20020830

Last Updated on STN: 20020830

AB Recent trials have established the IFL combination (fluorouracil [5-FU], leucovorin, and ***irinotecan*** [CPT-11, ***Camptosar***]) as a new standard first-line ***therapy*** for patients with metastatic ***colorectal*** cancer. Median survival for such patients ***treated*** with IFL still ranges from approximately 14 to 18 months, however, underscoring the need for new agents with novel mechanisms of action. Angiogenesis has become an attractive target for anticancer drug development, based on its important roles in tumor growth, invasion, and metastasis. A potent stimulus of angiogenesis is vascular endothelial growth factor (VEGF); two agents developed to inhibit VEGF activity, bevacizumab (Avastin) and SU5416, are in advanced clinical trials. Based on encouraging results in phase I and II trials with bevacizumab, a randomized trial of IFL with or without this ***monoclonal*** antibody is under way. Similarly, a randomized trial of 5-FU and leucovorin with or without the tyrosine kinase inhibitor SU5416 has recently completed accrual and results are pending. SU5416 is also being tested in a phase I/II trial combined with IFL. This article briefly reviews preclinical and clinical data leading to the current trials of these two agents in patients with ***colorectal*** cancer.

L40 ANSWER 22 OF 76 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:12588 CAPLUS

DOCUMENT NUMBER: 134:81772

TITLE: Stress-inducible GRP78 promoter and its use in gene

therapy

INVENTOR(S): Lee, Amy S.

PATENT ASSIGNEE(S): University of Southern California, USA

SOURCE: PCT Int. Appl., 121 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001000791	A1	20010104	WO 2000-US17885	20000628
WO 2001000791	C2	20020725		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1194527	A1	20020410	EP 2000-948536	20000628
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				

PRIORITY APPLN. INFO.: US 1999-141505P P 19990628

WO 2000-US17885 W 20000628

AB This invention relates to compns. and methods for selective expression of a heterologous nucleic acid sequence in a targeted tissue, and more particularly to the glucose regulated protein 78 (grp78) stress-responsive promoter and its use in gene ***therapy*** and the prodn. of transgenic animals. Thus, a retroviral vector contg. a herpes simplex virus thymidine kinase gene controlled by the rat GRP78 promoter was prepd. In B/C10ME cells (mouse mammary adenocarcinoma cells) contg. this vector, expression of the thymidine kinase gene was induced by glucose deprivation. The recombinant B/C10ME cells were injected into mice. After tumors had developed, ganciclovir was administered. Tumor regression was obsd. in these mice, unlike those injected with unaltered B/C10ME cells.

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L40 ANSWER 23 OF 76 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:314166 CAPLUS

DOCUMENT NUMBER: 134:325213

TITLE: Immunotherapy of B cell involvement in progression of
solid, nonlymphoid tumors

INVENTOR(S): Barbera-Guillem, Emilio

PATENT ASSIGNEE(S): Biocrystal Ltd., USA

SOURCE: U.S., 24 pp.

CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6224866	B1	20010501	US 1999-411116	19991004
EP 1127260	A1	20010829	EP 1999-970163	19991006
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
US 2001033839	A1	20011025	US 2001-835759	20010416
PRIORITY APPLN. INFO.: US 1998-103350P P 19981007				
US 1999-117526P P 19990128				
US 1999-411116 A2 19991004				
WO 1999-US23284 W 19991006				

AB A method for ***treating*** a pro-tumor immune response in an individual having, or suspected of having, a pro-tumor immune response, by administering a ***therapeutically*** effective amt. of an immunotherapeutic compn. which binds to a determinant on B cells, resulting in B cell depletion including of B cells that may be involved in promotion of tumor progression. Also provided are immunotherapeutic compns. which can be used for ***treating*** a pro-tumor immune response. The immunotherapeutic compns. comprise a ***chimeric*** anti-CD20 ***monoclonal*** antibody and chemotherapeutic agents and/or anti-inflammatory agents and/or cytolytic agents.

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L40 ANSWER 24 OF 76 MEDLINE

ACCESSION NUMBER: 2001671165 MEDLINE

DOCUMENT NUMBER: 21573729 PubMed ID: 11716702

TITLE: Identification and activities of human carboxylesterases
for the activation of CPT-11, a clinically approved
anticancer drug.

AUTHOR: Senter P D; Beam K S; Mixan B; Wahl A F

CORPORATE SOURCE: Seattle Genetics, Inc. 21823 30th Drive SE, Bothell,
Washington 98021, USA.. psenter@seagen.com

CONTRACT NUMBER: 1R43 CA85109-01 (NCI)

SOURCE: BIOCONJUGATE CHEMISTRY, (2001 Nov-Dec) 12 (6) 1074-80.
Journal code: 9010319. ISSN: 1043-1802.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200202

ENTRY DATE: Entered STN: 20011122

Last Updated on STN: 20020227

Entered Medline: 20020226

AB CPT-11 is a clinically approved anticancer drug used for the
treatment of advanced ***colorectal*** cancer. Upon
administration, the carbamate side chain of the drug is hydrolyzed,
resulting in the release of SN-38, an agent that has approximately
1000-fold increased cytotoxic activity. Since only a very small percentage
of the injected dose of CPT-11 is converted to SN-38, there is a

significant opportunity to improve its ***therapeutic*** efficacy and to diminish its systemic toxicity by selectively activating the drug within tumor sites. We envisioned that a ***mAb***-human enzyme conjugate for CPT-11 activation would be of interest, particularly since the conjugate would likely be minimally immunogenic, and the prodrug is clinically approved. Toward this end, it was necessary to identify the most active human enzyme that could convert CPT-11 to SN-38. We isolated enzymes from human liver microsomes based on their abilities to effect the conversion and identified human carboxylesterase 2 (hCE-2) as having the greatest specific activity. hCE-2 was 26-fold more active than human carboxylesterase 1 and was 65% as active as rabbit liver carboxylesterase, the most active CPT-11 hydrolyzing enzyme known. The anti-p97 ***mAb*** 96.5 was linked to hCE-2, forming a conjugate that could bind to antigen-positive cancer cells and convert CPT-11 to SN-38. Cytotoxicity assays established that the conjugate led to the generation of active drug, but the kinetics of prodrug activation ($48 \text{ pmol} \times \text{min}^{-1} \times \text{mg}^{-1}$) was insufficient for immunologically specific prodrug activation. These results confirm the importance of hCE-2 for CPT-11 activation and underscore the importance of enzyme kinetics for selective prodrug activation.

L40 ANSWER 25 OF 76 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.

ACCESSION NUMBER: 2001251670 EMBASE

TITLE: The type III epidermal growth factor receptor mutation.

Biological significance and potential target for anti-cancer therapy.

AUTHOR: Pedersen M.W.; Meltorn M.; Damstrup L.; Poulsen H.S.

CORPORATE SOURCE: Dr. H.S. Poulsen, Department of Radiation Biology, The Finsen Centre, National University Hospital, Blegdamsvej 9, 2100 Copenhagen, Denmark. Skovgaard@rh.dk

SOURCE: Annals of Oncology, (2001) 12/6 (745-760).

Refs: 106

ISSN: 0923-7534 CODEN: ANONE2

COUNTRY: Netherlands

DOCUMENT TYPE: Journal; General Review

FILE SEGMENT: 016 Cancer

022 Human Genetics

030 Pharmacology

037 Drug Literature Index

038 Adverse Reactions Titles

LANGUAGE: English

SUMMARY LANGUAGE: English

AB Mutations in the epidermal growth factor receptor occur frequently in a number of human tumours including gliomas, non-small-cell lung carcinomas, ovarian carcinomas and prostate carcinomas. The type III epidermal growth factor receptor mutation (variously named EGFRvIII, de2-7 ***EGFR*** or .DELTA. ***EGFR***), which lacks a portion of the extracellular ligand binding domain, is the most common. Here, we review the current status with regard to the role of EGFRvIII in human cancers. A detailed discussion of the formation of EGFRvIII and its structure at the protein level are likewise included along with a discussion of its more functional roles. The design and use (preclinical and clinical) of small molecule inhibitors, antibodies, and antisense oligonucleotides against wild-type ***EGFR*** are considered in detail as these strategies can be directly adapted to target EGFRvIII. Finally, the status of EGFRvIII targeted therapy is reviewed.

L40 ANSWER 26 OF 76 MEDLINE

ACCESSION NUMBER: 2001681577 MEDLINE

DOCUMENT NUMBER: 21584872 PubMed ID: 11727507

TITLE: IMC-C225, an anti-epidermal growth factor receptor

monoclonal antibody, for ***treatment*** of head and neck cancer.

AUTHOR: Herbst R S; Kim E S; Harari P M

CORPORATE SOURCE: Department of Thoracic & Head and Neck Medical Oncology, M.D. Anderson Cancer Center, 1515 Holcombe Boulevard, Houston, TX 77030, USA.. rherbst@mdanderson.org

SOURCE: Expert Opin Biol Ther, (2001 Jul) 1 (4) 719-32. Ref: 100

Journal code: 101125414. ISSN: 1471-2598.

PUB. COUNTRY: England; United Kingdom

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

General Review; (REVIEW)

(REVIEW, TUTORIAL)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200202

ENTRY DATE: Entered STN: 20011203

Last Updated on STN: 20020207

Entered Medline: 20020206

AB Squamous cell carcinoma (SCC) of the head and neck (H&N) remains a clinical challenge due to its high rate of locoregional disease recurrence. The importance of the epidermal growth factor receptor (***EGFR***) in the development and progression of many solid tumours (including SCC of the H&N) is well understood; increased expression is associated with enhanced tumour invasion, resistance to chemotherapy and decreased patient survival. Several approaches have been developed to achieve ***EGFR*** blockade as an anticancer ***treatment*** strategy, including an anti- ***EGFR*** ***monoclonal*** antibody (***mAb***), IMC-C225, which competitively binds to the extracellular receptor site to prevent binding by natural ***EGFR*** ligands (EGF and TGF- α). Preclinical studies evaluating this ***chimeric*** ***mAb*** in human cancer cell lines in vitro and human tumour xenografts in vivo have demonstrated its potent antitumour activity. The clinical efficacy of IMC-C225 appears to involve multiple anticancer mechanisms, including inhibition of cell cycle progression, induction of apoptosis, anti-angiogenesis, inhibition of metastasis and its ability to enhance the response to chemotherapy and radiation ***therapy***. Phase I studies of IMC-C225 combined with chemotherapy or radiation for SCC of the H&N demonstrate excellent response rates in patients with recurrent or refractory disease. Phase II and III trials examining the efficacy and safety of these combinations are currently underway. To date, IMC-C225 has been well-tolerated, with skin rashes and allergic reactions being the most clinically important adverse events reported. IMC-C225 displays dose-dependent elimination characteristics and a half-life of approximately 7 days. Current recommendations for dosing include a 400 mg/m² loading dose, followed by weekly infusions of 250 mg/m².

L40 ANSWER 27 OF 76 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: 2002:146833 BIOSIS

DOCUMENT NUMBER: PREV200200146833

TITLE: bcl-2/bax ratio as a predictive marker for
therapeutic response to radiotherapy in patients
with rectal cancer.

AUTHOR(S): Scopa, Chrisoula D. (1); Vagianos, Constantine; Kardamakis,
Dimitrios; Kourelis, Theodore G.; Kalofonos, Haralabos P.;
Tsamandas, Athanasios C.

CORPORATE SOURCE: (1) 261 10, Patras: cdsropa@med.upatras.gr Greece

SOURCE: Applied Immunohistochemistry & Molecular Morphology,
(December, 2001) Vol. 9, No. 4, pp. 329-334.
<http://www.appliedimmunohist.com/>. print.

DOCUMENT TYPE: Article

LANGUAGE: English

AB Combined radiation ***therapy*** and chemotherapy are adjuvant
treatments given after surgery to patients with rectal carcinoma.
Because apoptosis seems to play a role in tumor response to radiotherapy,
the current study investigates whether there is a correlation between the
ratio of bcl-2 oncoprotein and bax expression in rectal adenocarcinoma and
the clinical response to radiotherapy. Elective colectomy for primary
rectal adenocarcinoma followed by adjuvant radiotherapy and chemotherapy
was performed on 35 patients. Tumors were staged as B2 (n=30) and C (n=5),
and were classified as radiation resistant (n=19, group A) and radiation
nonresistant (n=16, group B). Immunohistochemical study, using the
streptavidin-biotin complex technique and ***monoclonal*** antibody to
bcl-2 and polyclonal antibody to bax protein was used on paraffin

sections. Cases were considered positive if at least 5% of tumor cells displayed cytoplasmic staining for bcl-2 or bax. In each tumor, the bcl-2/bax ratio was calculated dividing the percentage of bcl-2-positive cells by the percentage of bax-positive cells. For statistical analysis, the Mann-Whitney rank sum test and Kruskal-Wallis analysis of variance test were used. Rectal tumors of group A displayed significantly greater bcl-2 immunoreactivity (40.2+4.2) compared with group B (20.2+3.8). In contrast, expression of bax protein was less in group A (30.3+3.3) compared with group B (41.3+2.3). The bcl-2/bax ratio was greater in group A (1.3+0.1) compared with group B (0.49+0.1), and was correlated with poor responsiveness to radiotherapy. The current study indicates that in patients with rectal carcinoma an elevated bcl-2/bax ratio in tissue specimens suggests increased tumor resistance to adjuvant radiotherapy. Thus, in such patients, the bcl-2/bax ratio may serve as a potential molecular marker for prediction of tumor prognosis.

L40 ANSWER 28 OF 76 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: 2001:468718 BIOSIS

DOCUMENT NUMBER: PREV200100468718

TITLE: Growth inhibition of human ***colorectal*** carcinoma xenografts by anti-EGF receptor ***monoclonal*** antibody IMC-C225 in combination with 5-fluorouracil or ***irinotecan***.

AUTHOR(S): Prewett, Marie (1); Hooper, Andrea; Bassi, Rajiv; Ellis, Lee M.; Waksal, Harlan; Hicklin, Daniel J.

CORPORATE SOURCE: (1) ImClone Systems Incorporated, New York, NY USA

SOURCE: Proceedings of the American Association for Cancer Research Annual Meeting, (March, 2001) Vol. 42, pp. 287. print.
Meeting Info.: 92nd Annual Meeting of the American Association for Cancer Research New Orleans, LA, USA March 24-28, 2001
ISSN: 0197-016X.

DOCUMENT TYPE: Conference

LANGUAGE: English

SUMMARY LANGUAGE: English

L40 ANSWER 29 OF 76 MEDLINE

ACCESSION NUMBER: 2001571418 MEDLINE

DOCUMENT NUMBER: 21535133 PubMed ID: 11677653

TITLE: Radiation response modification following molecular inhibition of epidermal growth factor receptor signaling.

AUTHOR: Harari P M; Huang S M

CORPORATE SOURCE: Department of Human Oncology, University of Wisconsin Medical School and Comprehensive Cancer Center, Madison, WI 53792, USA.

SOURCE: SEMINARS IN RADIATION ONCOLOGY, (2001 Oct) 11 (4) 281-9.
Ref: 37
Journal code: 9202882. ISSN: 1053-4296.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200112

ENTRY DATE: Entered STN: 20011029

Last Updated on STN: 20020420

Entered Medline: 20011207

AB The epidermal growth factor receptor (***EGFR***) has emerged as a central molecular target for modulation in cancer ***therapeutics***. The correlation between overexpression of ***EGFR*** and clinically aggressive malignant disease renders ***EGFR*** a promising ***therapy*** target for many epithelial tumors, which represent approximately two thirds of all human cancers. Although the initial impetus for examining ***EGFR*** signal interruption as an anticancer strategy involved proliferative growth inhibition, more recent studies now confirm the capacity of ***EGFR*** down-regulation to modify

apoptosis, invasion capacity, angiogenesis, DNA damage repair, and cellular response to radiation and selected chemotherapy agents. The favorable interaction profile for ***EGFR*** blocking agents combined with radiation and/or chemotherapy has stimulated clinical trials in diverse anatomic sites including head and neck, ***colorectal***, pancreas, and lung. Among the most well studied and promising current agents for ***EGFR*** signal modulation are C225 and ZD1839. C225 is a ***chimeric*** ***monoclonal*** antibody to the ***EGFR*** (extracellular domain), whereas ZD1839 is a selective inhibitor of the ***EGFR*** -tyrosine kinase (cytoplasmic domain). The spectrum of cellular and biological effects that follow molecular blockade of the ***EGFR*** is enlarging and reflect the central role of this receptor in regulating epithelial cell behavior. Molecular inhibition of ***EGFR*** signaling in combination with radiation represents a highly promising investigational arena. A preview of current translational research efforts and early clinical trials focused primarily on radiation interaction is provided herein.

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L40 ANSWER 30 OF 76 MEDLINE
 ACCESSION NUMBER: 2001372510 MEDLINE
 DOCUMENT NUMBER: 21322220 PubMed ID: 11429486
 TITLE: New chemotherapy approaches in ***colorectal*** cancer.
 AUTHOR: Grothey A; Schmoll H J
 CORPORATE SOURCE: Department of Hematology and Oncology, University of Halle, Halle, Germany.
 SOURCE: CURRENT OPINION IN ONCOLOGY, (2001 Jul) 13 (4) 275-86.
 Ref: 71
 Journal code: 9007265. ISSN: 1040-8746.
 PUB. COUNTRY: United States
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 General Review; (REVIEW)
 (REVIEW, TUTORIAL)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 200108
 ENTRY DATE: Entered STN: 20010820
 Last Updated on STN: 20010820
 Entered Medline: 20010816

AB ***Colorectal*** cancer is one of the leading causes of cancer deaths in the Western world, with approximately 50% of all patients dying from metastatic disease. Until recently, ***therapeutic*** options for advanced ***colorectal*** cancer were mainly confined to chemotherapy with 5-fluorouracil in various schedules, with or without biochemical modulation with leucovorin. The development of new cytotoxic drugs with substantial activity in this tumor during the past 2 years has dramatically changed ***treatment*** strategies and ***therapeutic*** goals in metastatic ***colorectal*** cancer and has introduced neoadjuvant chemotherapy followed by secondary surgery with the intent of long-term survival. Among these new drugs, oral fluoropyrimidines (tegafur/uracil and capecitabine), ***irinotecan***, and oxaliplatin have already established themselves as part of various ***treatment*** approaches. Other novel ***therapeutics*** including agents designed to act on molecular targets already show promising activity and will become part of combination protocols with current standard chemotherapy.

L40 ANSWER 31 OF 76 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
 ACCESSION NUMBER: 2002:289234 BIOSIS
 DOCUMENT NUMBER: PREV200200289234
 TITLE: Antibody blockade of the epidermal growth factor receptor combined with radiation.
 AUTHOR(S): Harari, P. (1); Huang, S. (1)
 CORPORATE SOURCE: (1) Department of Human Oncology, University of Wisconsin, Madison, WI USA
 SOURCE: European Journal of Cancer, (October, 2001) Vol. 37, No. Supplement 6, pp. S249. <http://www.elsevier.com/locate/ejca>

. print.

Meeting Info.: 11th European Cancer Conference Lisbon,
Portugal October 21-25, 2001
ISSN: 0959-8049.

DOCUMENT TYPE: Conference
LANGUAGE: English

L40 ANSWER 32 OF 76 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.

ACCESSION NUMBER: 2001202702 EMBASE

TITLE: Epidermal growth factor receptor as a target: Recent
developments in the search for effective new anti-cancer
agents.

AUTHOR: Seymour L.K.

CORPORATE SOURCE: L.K. Seymour, Investigational New Drug Program, Natl. Can.
Inst. Canada Clin. Trials, Queens University, 18 Barrie
Street, Kingston, Ont. K7L 3N6, Canada.
lseymour@ctg.queensu.ca

SOURCE: Current Drug Targets, (2001) 2/2 (117-133).

Refs: 108

ISSN: 1389-4501 CODEN: CDTUAU

COUNTRY: Netherlands

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 016 Cancer

030 Pharmacology

037 Drug Literature Index

038 Adverse Reactions Titles

LANGUAGE: English

SUMMARY LANGUAGE: English

AB A number of cancer chemotherapeutics targeting the epidermal growth factor
receptor (***EGFR***) are in development. These compounds were
designed to either bind to the ***EGFR*** or inhibit signal
transduction after receptor activation. Classes of inhibitory compounds
include small molecules and ***humanized*** ***monoclonal***
antibodies. Many of these compounds are relatively far advanced in
development. Proof of principle, with evidence of anti-tumour activity and
inhibition of ***EGFR*** activation/phosphorylation, has already been
demonstrated in some instances. Although these new compounds offer
exciting opportunities, they bring with them real challenges in terms of
the selection of appropriate trial designs as well as surrogate endpoints.

L40 ANSWER 33 OF 76 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.

ACCESSION NUMBER: 2001081564 EMBASE

TITLE: The anti-idiotypic vaccines for immunotherapy.

AUTHOR: Bhattacharya-Chatterjee M.; Chatterjee S.K.; Foon K.A.

CORPORATE SOURCE: M. Bhattacharya-Chatterjee, Department of Internal
Medicine, The Barrett Cancer Center, University of
Cincinnati, Cincinnati, OH 45267-0509, United States.
malaya.chatterjee@uc.edu

SOURCE: Current Opinion in Molecular Therapeutics, (2001) 3/1
(63-69).

Refs: 33

ISSN: 1464-8431 CODEN: CUOTFO

COUNTRY: United Kingdom

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 016 Cancer

026 Immunology, Serology and Transplantation

030 Pharmacology

037 Drug Literature Index

038 Adverse Reactions Titles

LANGUAGE: English

SUMMARY LANGUAGE: English

AB Certain anti-idiotypic antibodies that bind to the antigen-combining sites
of antibodies can effectively mimic the three-dimensional structures and
functions of the external antigens and can be used as surrogate antigens
for active specific immunotherapy. Extensive studies in animal models have
demonstrated the efficacy of these vaccines for triggering the immune
system to induce specific and protective immunity against bacterial, viral

and parasitic infections as well as tumors. Several ***monoclonal*** anti-idiotypic antibodies that mimic distinct human tumor-associated antigens have been developed and characterized. Encouraging results have been obtained in recent clinical trials using these anti-idiotypic antibodies as vaccines. In this article, we will review the current literature and discuss the potential of this novel ***therapeutic*** approach for various human cancers.

L40 ANSWER 34 OF 76 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.

ACCESSION NUMBER: 2001330958 EMBASE

TITLE: Targeting the epidermal growth factor receptor: A clinical reality.

AUTHOR: Baselga J.

CORPORATE SOURCE: Dr. J. Baselga, Vall d'Hebron University Hospital, P Vall D'Hebron 119-129, 08035 Barcelona, Spain.
baselga@hg.vhebron.es

SOURCE: Journal of Clinical Oncology, (15 Sep 2001) 19/18 SUPPL. (41s-44s).

Refs: 11

ISSN: 0732-183X CODEN: JCONDN

COUNTRY: United States

DOCUMENT TYPE: Journal; Conference Article

FILE SEGMENT: 016 Cancer

030 Pharmacology

037 Drug Literature Index

LANGUAGE: English

L40 ANSWER 35 OF 76 MEDLINE

ACCESSION NUMBER: 2002257102 MEDLINE

DOCUMENT NUMBER: 21984979 PubMed ID: 11995705

TITLE: [***Colorectal*** cancer: ***irinotecan*** in combination with newer drugs].
Carcinoma del colon-retto: ***irinotecan*** in combinazione con i nuovi farmaci.

AUTHOR: Falcone A

SOURCE: TUMORI, (2001 Nov-Dec) 87 (6) A31-3. Ref: 28
Journal code: 0111356. ISSN: 0300-8916.

PUB. COUNTRY: Italy

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)

LANGUAGE: Italian

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200205

ENTRY DATE: Entered STN: 20020509

Last Updated on STN: 20020518

Entered Medline: 20020517

L40 ANSWER 36 OF 76 MEDLINE

ACCESSION NUMBER: 2001422898 MEDLINE

DOCUMENT NUMBER: 21197388 PubMed ID: 11301838

TITLE: Future directions in adjuvant ***therapy*** for stage III colon carcinoma.

AUTHOR: Pitot H C; Goldberg R M

CORPORATE SOURCE: Division of Medical Oncology, Mayo Cancer Center, Gastrointestinal Cancer Research Program, Mayo Clinic, Rochester, Minnesota, USA.

SOURCE: ONCOLOGY, (2001 Mar) 15 (3 Suppl 5) 31-6. Ref: 31
Journal code: 8712059. ISSN: 0890-9091.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200107

ENTRY DATE: Entered STN: 20010730

Last Updated on STN: 20010730

Entered Medline: 20010726

AB The current recommendation for adjuvant chemotherapy for patients with newly diagnosed stage III colon cancer involves 6 months of fluorouracil (5-FU) plus low- or high-dose leucovorin. In clinical trials performed throughout the world, several drugs have demonstrated either improved toxicity profiles or antitumor activity for patients with advanced ***colorectal*** carcinoma. Uracil and tegafur (UFT) and capecitabine (Xeloda) are two examples of new oral chemotherapy compounds with acceptable side-effect profiles in early adjuvant or advanced disease trials. ***Irinotecan*** (CPT-11, ***Camptosar***) and oxaliplatin, when administered intravenously in combination with a 5-FU regimen, have both demonstrated significant antitumor effects for patients with advanced-stage disease. Other immunotherapies, including ***monoclonal*** antibodies and cancer vaccines, are being evaluated to help stimulate immune responses in patients with resected colon cancer. These agents are just a few examples of the new compounds being tested in the next generation of clinical trials for resected stage III colon cancer. Future and ongoing investigations will look to integrate these new ***therapies*** as we attempt to move beyond the era of 5-FU and leucovorin.

L40 ANSWER 37 OF 76 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.

ACCESSION NUMBER: 2001225629 EMBASE

TITLE: New targets, new drugs highlight oncology meeting.

AUTHOR: McCann J.

SOURCE: Drug Topics, (4 Jun 2001) 145/11 (27).

ISSN: 0012-6616 CODEN: DGTNA7

COUNTRY: United States

DOCUMENT TYPE: Journal; (Short Survey)

FILE SEGMENT: 016 Cancer

037 Drug Literature Index

LANGUAGE: English

L40 ANSWER 38 OF 76 MEDLINE

ACCESSION NUMBER: 2001551268 MEDLINE

DOCUMENT NUMBER: 21481779 PubMed ID: 11597400

TITLE: The ***EGFR*** as a target for anticancer

therapy --focus on cetuximab.

AUTHOR: Baselga J

CORPORATE SOURCE: Medical Oncology Service, Hospital General Universitari

Vall d'Hebron, Paseo Vall d'Hebron 119-129, 08035,

Barcelona, Spain.. baselga@hg.vhebron.es

SOURCE: EUROPEAN JOURNAL OF CANCER, (2001 Sep) 37 Suppl 4 S16-22.

Ref: 45

Journal code: 9005373. ISSN: 0959-8049.

PUB. COUNTRY: England: United Kingdom

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

General Review; (REVIEW)

(REVIEW, TUTORIAL)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200112

ENTRY DATE: Entered STN: 20011015

Last Updated on STN: 20020122

Entered Medline: 20011207

AB The anti-epidermal-growth-factor-receptor (***EGFR***)

monoclonal antibody cetuximab specifically binds to the ***EGFR*** with high affinity, blocking growth-factor binding, receptor activation and subsequent signal-transduction events leading to cell proliferation. Preclinical studies, both in vitro and in vivo, have shown that cetuximab enhances the antitumour effects of chemotherapy as well as radiotherapy by inhibiting cell proliferation, angiogenesis and metastasis and by promoting apoptosis. As of June 2000, 526 patients with advanced solid tumours were ***treated*** with cetuximab in phase I/II clinical trials. Analysis of the results of three phase I trials showed that cetuximab has non-linear pharmacokinetics, with saturation of

drug-elimination pathways occurring at doses between 200 and 400 mg/m(2). Adverse-event data for 239 patients across most of the completed or ongoing phase I-III trials indicated that the antibody was generally well tolerated. Cetuximab has been evaluated both alone and in combination with radiotherapy and various cytotoxic chemotherapeutic agents in a series of phase I/II studies that primarily ***treated*** patients with either head and neck or ***colorectal*** cancer. Although not a primary objective of these studies, clinical responses to cetuximab were observed in many patients who had previously failed chemotherapy and/or radiotherapy or were otherwise unlikely to achieve a ***therapeutic*** outcome. Based on these promising results, additional phase II and phase III trials are currently underway in head and neck and ***colorectal*** cancer.

L40 ANSWER 39 OF 76 MEDLINE

ACCESSION NUMBER: 2001141186 MEDLINE

DOCUMENT NUMBER: 21098144 PubMed ID: 11167991

TITLE: Influence of cytokines, ***monoclonal*** antibodies and chemotherapeutic drugs on epithelial cell adhesion molecule (EpCAM) and LewisY antigen expression.

AUTHOR: Flieger D; Hoff A S; Sauerbruch T; Schmidt-Wolf I G

CORPORATE SOURCE: Medizinische Klinik und Poliklinik I, Allgemeine Innere Medizin, Universitat Bonn, Bonn, Germany. D..
Flieger@uni-bonn.de

SOURCE: CLINICAL AND EXPERIMENTAL IMMUNOLOGY, (2001 Jan) 123 (1) 9-14.

Journal code: 0057202. ISSN: 0009-9104.

PUB. COUNTRY: England; United Kingdom

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200103

ENTRY DATE: Entered STN: 20010404

Last Updated on STN: 20010404

Entered Medline: 20010308

AB MoAbs against tumour-associated antigens (TAA) may be useful for the ***treatment*** of ***colorectal*** cancer. Since an increased expression of TAA may lead to enhanced antibody-dependent cellular cytotoxicity we examined whether the cytokines IL-2, IL-4, IL-6, IL-10, IL-12, interferon-alpha (IFN-alpha), IFN-gamma, granulocyte-macrophage colony-stimulating factor, macrophage colony-stimulating factor and tumour necrosis factor-alpha can influence EpCAM and LewisY expression on the surface of the ***colorectal*** carcinoma cell lines HT29, LoVo and SW480. We found that only IFN-alpha increased significantly whereas IL-4 decreased both EpCAM and LewisY expression. IFN-gamma significantly increased LewisY expression only. When tumour cells were ***treated*** with MoAb, the LewisY-specific MoAb BR55-2 down-regulated LewisY antigen expression, whereas MoAb 17-1A, which binds to EpCAM, up-regulated this TAA after 3 days of culture. The cytokines IFN-alpha or IFN-gamma combined with MoAb 17-1A enhanced further slightly the expression of EpCAM. In additional experiments with chemotherapeutic drugs commonly used for the ***treatment*** of ***colorectal*** cancer, we found that 5-fluorouracil, mitomycin-C and oxaliplatin up-regulated EpCAM and LewisY antigen expression. Raltitrexed enhanced LewisY and down-regulated EpCAM expression, whereas CPT-11 had no influence at all. The highest expression for EpCAM on HT29 cells was achieved by the combination of IFN-alpha, 5-fluorouracil and MoAb 17-1A. Our results may be useful for defining combinations of biological and chemotherapeutic drugs for the ***treatment*** of ***colorectal*** cancer. Further trials should evaluate to what extent these combinations enhance antibody-dependent cellular cytotoxicity.

L40 ANSWER 40 OF 76 MEDLINE

ACCESSION NUMBER: 2000399270 MEDLINE

DOCUMENT NUMBER: 20393605 PubMed ID: 10939611

TITLE: [Last news from ASCO 2000 in the topic of
colorectal cancer].

Ultime novità dall'ASCO 2000 in tema di carcinoma del colon-retto.

AUTHOR: Sobrero A
 CORPORATE SOURCE: Oncologia medica, Università di Udine.
 SOURCE: TUMORI, (2000 May-Jun) 86 (3) A1-2.
 Journal code: 0111356. ISSN: 0300-8916.
 PUB. COUNTRY: Italy
 DOCUMENT TYPE: News Announcement
 LANGUAGE: Italian
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 200008
 ENTRY DATE: Entered STN: 20000824
 Last Updated on STN: 20001019
 Entered Medline: 20000816

L40 ANSWER 41 OF 76 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
 ACCESSION NUMBER: 2000333458 EMBASE
 TITLE: Docetaxel-induced lymphopenia in patients with solid tumors: A prospective phenotypic analysis.
 AUTHOR: Kotsakis A.; Sarra E.; Peraki M.; Koukourakis M.; Apostolaki S.; Souglakos J.; Mavromanakis E.; Vlachonikolis J.; Georgoulas V.
 CORPORATE SOURCE: Dr. V. Georgoulas, Department of Medical Oncology, Univ. General Hospital of Heraklion, P.O. Box 1352, 71110 Heraklion, Crete, Greece. georgoul@med.uch.gr
 SOURCE: Cancer, (15 Sep 2000) 89/6 (1380-1386).
 Refs: 27
 ISSN: 0008-543X CODEN: CANCAR
 COUNTRY: United States
 DOCUMENT TYPE: Journal; Article
 FILE SEGMENT: 016 Cancer
 037 Drug Literature Index
 038 Adverse Reactions Titles
 LANGUAGE: English
 SUMMARY LANGUAGE: English

AB BACKGROUND. The quantitative abnormalities of the different peripheral blood lymphocyte subsets during docetaxel administration were prospectively studied. METHODS. Forty-six chemotherapy-naïve patients with solid tumors were ***treated*** with docetaxel either in a 3 weekly (n = 33) or weekly (n = 13) schedule. Twenty patients with central nervous system (CNS) metastatic disease as the first clinical presentation of cancer and 35 patients with metastatic ***colorectal*** carcinoma ***treated*** with chemotherapy were enrolled as controls. The phenotype of peripheral blood lymphocytes was determined by indirect immunofluorescence using appropriate ***monoclonal*** antibodies and fluorescent-activated cell sorter analysis. RESULTS. After the administration of the first docetaxel cycle, the absolute number of peripheral blood lymphocytes (P < 0.005), CD3+ (P < 0.01), CD4+ (P < 0.01), CD8+ (P < 0.01), and CD56+ (P < 0.01) but not CD20+ (P < 0.3) cells was significantly decreased compared with the pretreatment values. Further ***treatment*** resulted in a further decrease of these lymphocyte subsets including CD20+ cells (P < 0.01). Similarly, after the administration of the first weekly dose of docetaxel, the absolute number of total lymphocytes, CD3+, CD4+, and CD8+ cells was decreased. The administration of the second weekly docetaxel dose resulted in a further decrease of CD56+ (P = 0.012) and CD20+ (P = 0.007) cells. The administration of either high dose corticosteroids in patients with CNS metastases or an irrelevant chemotherapy (CPT-11/5-FU) did not result in similar abnormalities. The discontinuation of docetaxel was associated with a recovery of CD3+ and CD4+ lymphocytes within a 3-month period. Eight (17%) patients developed nonneutropenic infections during docetaxel ***treatment***. CONCLUSIONS. Docetaxel has an important but reversible nonspecific lymphopenic effect that seems to be associated with an increased risk for nonneutropenic infections. (C) 2000 American Cancer Society.

L40 ANSWER 42 OF 76 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.

ACCESSION NUMBER: 2000339683 EMBASE
 TITLE: CEA-Cide Immunomedics Inc.
 AUTHOR: Smith S.V.
 CORPORATE SOURCE: S.V. Smith, PO Box 849, Sutherland, NSW 1499, Australia
 SOURCE: Current Opinion in Oncologic, Endocrine and Metabolic
 Investigational Drugs, (2000) 2/4 (414-422).
 Refs: 73
 ISSN: 1464-8466 CODEN: COODF2
 COUNTRY: United Kingdom
 DOCUMENT TYPE: Journal; General Review
 FILE SEGMENT: 037 Drug Literature Index
 030 Pharmacology
 016 Cancer
 015 Chest Diseases, Thoracic Surgery and Tuberculosis
 048 Gastroenterology
 003 Endocrinology
 038 Adverse Reactions Titles
 LANGUAGE: English

L40 ANSWER 43 OF 76 MEDLINE
 ACCESSION NUMBER: 2000491369 MEDLINE
 DOCUMENT NUMBER: 20496535 PubMed ID: 11043819
 TITLE: Progress in ***colorectal*** cancer chemotherapy: how
 far have we come, how far to go?
 AUTHOR: Royce M E; Hoff P M; Pazdur R
 CORPORATE SOURCE: University of Texas, M. D. Anderson Cancer Center, Division
 of Medicine, Houston 77030, USA.
 SOURCE: DRUGS AND AGING, (2000 Sep) 17 (3) 201-16. Ref: 91
 Journal code: 9102074. ISSN: 1170-229X.
 PUB. COUNTRY: New Zealand
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 General Review; (REVIEW)
 (REVIEW, TUTORIAL)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 200102
 ENTRY DATE: Entered STN: 20010322
 Last Updated on STN: 20010322
 Entered Medline: 20010202

AB Fluorouracil has been the mainstay of ***treatment*** for
 colorectal cancer (CRC) for almost 40 years. Various schedules and
 biochemical modulators have been investigated in an attempt to improve the
 therapeutic efficacy of fluorouracil. To date, fluorouracil plus
 folinic acid represents the standard ***therapy*** in CRC for the
 adjuvant ***treatment*** of patients at high risk for relapse and for
 the first-line ***treatment*** of metastatic disease. To gain clinical
 acceptance, however, oral fluoropyrimidines must confer at least the same
 survival advantages associated with the optimal intravenous fluorouracil
 regimens. ***Irinotecan*** and oxaliplatin are 2 other novel agents
 that have mechanisms of action that are uniquely different from those of
 fluorouracil, with demonstrated activity in patients with
 fluorouracil-refractory disease. Recent randomised trials comparing
 fluorouracil plus folinic acid with combinations of either
 irinotecan or oxaliplatin and fluorouracil plus folinic acid have
 shown that response rates are improved and time to progression is
 increased in patients receiving the combination regimens. These regimens
 are being rapidly introduced in the adjuvant setting, and the role and
 acceptance of these combination regimens as first-line ***therapy***
 needs to be defined. Other novel agents being evaluated in the
 treatment of patients with advanced CRC include oral edrecolomab (
 monoclonal antibody 17-1A) and tumour vaccines. Future research is
 focused on enabling clinicians to individualise ***treatment***
 strategies in patients with CRC, so as to improve clinical outcomes and
 reduce drug toxicity.

L40 ANSWER 44 OF 76 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 2000:656249 CAPLUS

DOCUMENT NUMBER: 133:249034
 TITLE: Anti-CEA-immunoradiation (131I-Anti-CEA-Ak F023C5 and MN-14) vs. conventional chemotherapy (LV/5-FU and ***irinotecan***) in the ***therapy*** of ***colorectal*** metastases in nude mice model
 AUTHOR(S): Liersch, T.; Behr, Th.; Gratz, S.; Fayyazi, A.; Becker, W.; Becker, H.
 CORPORATE SOURCE: Abteilung Allgemeinchirurgie, Universitätsklinik Goettingen, Germany
 SOURCE: Chirurgisches Forum fuer Experimentelle und Klinische Forschung (2000) 143-147
 CODEN: CFEKA7; ISSN: 0303-6227
 PUBLISHER: Springer-Verlag
 DOCUMENT TYPE: Journal
 LANGUAGE: German

AB At the time of Ro resection of ***colorectal*** cancer, occult micrometastases are present in >50% of the patients, and seem to be the limiting factor for overall survival. Esp. the liver is the most frequent site of apparent metastatic disease. Frequently, adjuvant chemotherapy is unable to prevent cancer recurrence. Thus, beyond std. chemotherapy like leucovorin (LV)/5-FU or ***irinotecan***, new ***therapeutic*** strategies like the anti-CEA-radioimmunotherapy (RAIT) are warranted. In this study the authors aimed to establish a model of human colon cancer metastatic to the liver of nude mice to assess the ***therapeutic*** efficacy of the radioimmunotherapy with the ***monoclonal*** 131I-labeled murine anti-CEA-IgG, antibody (***Mab***) Fo23C5 and with the anti-CEA ***Mab***, MN-14, compared to std. chemotherapy with LV/5-FU or ***irinotecan***. Multiple liver metastases of the colon cancer cell line, GW-39, were induced by intrasplenic injection of a 10% tumor cell suspension. Whereas controls were left untreated, the RAIT was initiated on day 10 or 20 after tumor inoculation with the low-affinity anti-CEA ***Mab***, Fo23C5 ($K_a=107$ l/mol), or the high-affinity-anti-CEA ***Mab***, MN-14 ($K_a=109$ l/mol), or chemotherapy at their resp. maximally tolerated doses (MTD). After 6.5 mo all surviving mice were killed and histol. investigated. After tumor inoculation the untreated controls died from rapidly progressing hepatic metastases at 6-8 wk. The lifespan of mice ***treated*** with LV/5-FU was prolonged by only 1-3 wk, whereas ***irinotecan*** led to a 5-8 wk prolongation of survival. In contrast, at their MTDs, Fo23C5 led to a <20% and the high-affinity ***Mab***, MN-14, to an 80% permanent cure rate, when initiating ***therapy*** at 10 days after tumor inoculation. In the 20-day-old metastatic stage, although prolonging life, Fo23C5 was unable to achieve cures, whereas MN-14 was successful in 20% of cases. Histol., no remaining viable cancer cells could be demonstrated in these animals surviving >6 mo. These data suggest that, in small-vol. disease, RAIT may be superior to std. chemotherapy. After RAIT the response rates in nude mice are better than with conventional chemotherapy, but with fewer side-effects. In particular, ongoing phase I/II studies with MAbs of higher affinity like the ***humanized*** MN-14 (hMN-14) will demonstrate the ***therapeutic*** efficacy in patients with metastatic ***colorectal*** cancer.

REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L40 ANSWER 45 OF 76 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.

ACCESSION NUMBER: 2000206359 EMBASE

TITLE: ***Irinotecan*** in second-line ***therapy*** of metastatic ***colorectal*** cancer.

CORPORATE SOURCE: Dr. A. Knuth, II. Medizinische Klinik, Krankenhaus Nordwest, Steinbacher Hohl 2-26, D-60488 Frankfurt/Main

SOURCE: Onkologie, (2000) 23/SUPPL. 4 (15-17).

Refs: 9

ISSN: 0378-584X CODEN: ONKOD2

COUNTRY: Germany

DOCUMENT TYPE: Journal; General Review

FILE SEGMENT: 016 Cancer

037 Drug Literature Index

038 Adverse Reactions Titles
 048 Gastroenterology
 LANGUAGE: English

L40 ANSWER 46 OF 76 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1999:48609 CAPLUS

DOCUMENT NUMBER: 130:119591

TITLE: Antioxidant enhancement of ***therapy*** for
 hyperproliferative conditions

INVENTOR(S): Chinery, Rebecca; Beauchamp, R. Daniel; Coffey, Robert
 J.; Medford, Russell M.; Wadsinski, Brian

PATENT ASSIGNEE(S): Atherogenics, Inc., USA

SOURCE: PCT Int. Appl., 112 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9901118	A2	19990114	WO 1998-US13750	19980701
WO 9901118	A3	19990422		
W: AL, AU, BA, BB, BG, BR, CA, CN, CU, CZ, EE, GE, HU, ID, IL, IS, JP, KP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9882827	A1	19990125	AU 1998-82827	19980701
EP 1019034	A2	20000719	EP 1998-933078	19980701
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002511878	T2	20020416	JP 1999-507360	19980701
US 2001049349	A1	20011206	US 2001-779086	20010207
PRIORITY APPLN. INFO.: US 1997-886653 A 19970701				
US 1997-967492 A 19971111				
US 1998-108609 B1 19980701				
WO 1998-US13750 W 19980701				

OTHER SOURCE(S): MARPAT 130:119591

AB A method to enhance the cytotoxic activity of an antineoplastic drug comprises administering an effective amt. of the antineoplastic drug to a host exhibiting abnormal cell proliferation in combination with an effective cytotoxicity-increasing amt. of an antioxidant. The invention also includes a method to decrease the toxicity to an antineoplastic agent or increase the ***therapeutic*** index of an antineoplastic agent administered for the ***treatment*** of a solid growth of abnormally proliferating cells, comprising administering an antioxidant prior to, with, or following the antineoplastic ***treatment***.

L40 ANSWER 47 OF 76 MEDLINE

ACCESSION NUMBER: 2000007382 MEDLINE

DOCUMENT NUMBER: 20007382 PubMed ID: 10541369

TITLE: Radioimmunotherapy of small volume disease of
 colorectal cancer metastatic to the liver:
 preclinical evaluation in comparison to standard
 chemotherapy and initial results of a phase I clinical
 study.

AUTHOR: Behr T M; Salib A L; Liersch T; Behe M; Angerstein C;
 Blumenthal R D; Fayyazi A; Sharkey R M; Ringe B; Becker H;
 Wormann B; Hiddemann W; Goldenberg D M; Becker W

CORPORATE SOURCE: Department of Nuclear Medicine, Georg-August-University of
 Gottingen, Germany.. tmbehr@med.uni-goettingen.de

CONTRACT NUMBER: CA 54425 (NCI)

CA39841 (NCI)

SOURCE: CLINICAL CANCER RESEARCH, (1999 Oct) 5 (10 Suppl)

3232s-3242s.

Journal code: 9502500. ISSN: 1078-0432.

PUB. COUNTRY: United States

DOCUMENT TYPE: (CLINICAL TRIAL)

(CLINICAL TRIAL, PHASE I)

Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199911

ENTRY DATE: Entered STN: 20000111

Last Updated on STN: 20000111

Entered Medline: 19991124

AB At the time of surgery, occult metastases (micrometastases) are present in more than 50% of ***colorectal*** cancer patients, and the liver is the most frequent site of apparent metastatic disease. Frequently, adjuvant chemotherapy is unable to prevent tumor recurrence. Thus, novel ***therapeutic*** strategies are warranted. The aim of this study was to establish a model of human colon cancer metastatic to the liver of nude mice, to assess, in this setting, the ***therapeutic*** efficacy of radioimmunotherapy (RAIT) compared to standard chemotherapy and to evaluate, in a Phase I/II trial, the toxicity and ***therapeutic*** efficacy of RAIT in ***colorectal*** cancer patients with small volume disease metastatic to the liver. Multiple liver metastases of the human colon cancer cell line GW-39 were induced by intrasplenic injection of a 10% tumor cell suspension. Whereas controls were left untreated, ***therapy*** was initiated on day 10 or 20 after tumor inoculation with the 131I-labeled, low affinity anticarcinoembryonic antigen (anti-CEA) ***monoclonal*** antibody (***MAb***), F023C5 (Ka = 10(7) liters/mol), or the high-affinity anti-CEA ***MAb***, MN-14 (Ka = 10(9) liters/mol), or chemotherapy (5-fluorouracil/leucovorin (folinic acid) versus ***irinotecan***) at their respective maximum tolerated doses (MTDs). Twelve ***colorectal*** cancer patients with small volume disease metastatic to the liver (all lesions \leq 2.5 cm) were entered into a mCi/m2-based Phase I dose escalation study with 131I-labeled ***humanized*** version of MN-14, hMN-14. The patients were given single injections, starting at 50 mCi/m2 and escalating in 10-mCi/m2 increments. The MTD was defined as the dose level at which \leq 1 of 6 patients develop grade 4 myelotoxicity. In the mice, untreated controls died from rapidly progressing hepatic metastases at 6-8 weeks after tumor inoculation. The life span of mice ***treated*** with 5-fluorouracil/leucovorin was prolonged for only 1-3 weeks, whereas ***irinotecan*** led to a 5-8-week prolongation. In contrast, at their respective MTDs, the 131I-labeled low-affinity anti-CEA ***MAb***, F023C5, led to a 20% permanent cure rate, and the high affinity ***MAb***, MN-14, led to an 80% permanent cure rate, when ***therapy*** was initiated at 10 days after tumor inoculation. In the 20-day-old tumor stage, although it prolonged life, 131I-F023C5 was unable to achieve cures, whereas 131I-MN-14 was still successful in 20%. Histologically, no remaining viable tumor cells could be demonstrated in these animals surviving $>$ 6 months. In patients, the MTD was reached at 60 mCi/m2 of hMN-14 (at 70 mCi/m2, two of three grade 4 myelotoxicities). Of 11 assessable patients, 2 had partial remissions (corresponding to an objective response rate of 18%), and 5 (45%) had minor/mixed responses or experienced stabilization of previously rapidly progressing disease. These data suggest that in small volume disease, RAIT may be superior to conventional chemotherapy. Antibodies of higher affinity seem to be clearly superior. The clinical response rates in patients with small volume disease are encouraging, being comparable to the response rates of conventional chemotherapeutic regimens but with fewer side effects. Ongoing studies will show whether ***treatment*** at the MTD will further improve ***therapeutic*** results.

L40 ANSWER 48 OF 76 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1999:740259 CAPLUS

DOCUMENT NUMBER: 131:319705

TITLE: Radioimmunotherapy of small volume disease of

colorectal cancer metastatic to the liver:

preclinical evaluation in comparison to standard chemotherapy and initial results of a Phase I clinical study

AUTHOR(S): Behr, Thomas M.; Salib, Alexandra L.; Liersch, Torsten; Behe, Martin; Angerstein, Christa; Blumenthal, Rosalyn D.; Fayyazi, Afshin; Sharkey, Robert M.; Ringe, Bernhard; Becker, Heinz; Wormann, Bernhard; Hiddemann, Wolfgang; Goldenberg, David M.; Becker, Wolfgang

CORPORATE SOURCE: Departments of Nuclear Medicine, Georg-August-University of Göttingen, Göttingen, D-37075, Germany

SOURCE: Clinical Cancer Research (1999), 5(10, Suppl.), 3232s-3242s

CODEN: CCREF4; ISSN: 1078-0432

PUBLISHER: American Association for Cancer Research

DOCUMENT TYPE: Journal

LANGUAGE: English

AB At the time of surgery, occult metastases (micrometastases) are present in more than 50% of ***colorectal*** cancer patients, and the liver is the most frequent site of apparent metastatic disease. Frequently, adjuvant chemotherapy is unable to prevent tumor recurrence. Thus, novel ***therapeutic*** strategies are warranted. The aim of this study was to establish a model of human colon cancer metastatic to the liver of nude mice, to assess, in this setting, the ***therapeutic*** efficacy of radioimmunotherapy (RAIT) compared to std. chemotherapy and to evaluate, in a Phase I/II trial, the toxicity and ***therapeutic*** efficacy of RAIT in ***colorectal*** cancer patients with small vol. disease metastatic to the liver. Multiple liver metastases of the human colon cancer cell line GW-39 were induced by intrasplenic injection of a 10% tumor cell suspension. Whereas controls were left untreated, ***therapy*** was initiated on day 10 or 20 after tumor inoculation with the 131I-labeled, low affinity anticarcinoembryonic antigen (anti-CEA) ***monoclonal*** antibody (***Mab***), F023C5 (Ka = 107 liters/mol), or the high-affinity anti-CEA ***Mab*** , MN-14 (Ka = 109 liters/mol), or chemotherapy (5-fluorouracil/leucovorin (folinic acid) vs. ***irinotecan***) at their resp. max. tolerated doses (MTDs). Twelve ***colorectal*** cancer patients with small vol. disease metastatic to the liver (all lesions .ltoreq.2.5 cm) were entered into a mCi/m2-based Phase I dose escalation study with 131I-labeled ***humanized*** version of MN-14, hMN-14. The patients were given single injections, starting at 50 mCi/m2 and escalating in 10-mCi/m2 increments. The MTD was defined as the dose level at which .ltoreq.1 of 6 patients develop grade 4 myelotoxicity. In the mice, untreated controls died from rapidly progressing hepatic metastases at 6-8 wk after tumor inoculation. The life span of mice ***treated*** with 5-fluorouracil/leucovorin was prolonged for only 1-3 wk, whereas ***irinotecan*** led to a 5-8-wk prolongation. In contrast, at their resp. MTDs, the 131I-labeled low-affinity anti-CEA ***Mab*** , F023C5, led to a 20% permanent cure rate, and the high affinity ***Mab*** , MN-14, led to an 80% permanent cure rate, when ***therapy*** was initiated at 10 days after tumor inoculation. In the 20-day-old tumor stage, although it prolonged life, 131I-F023C5 was unable to achieve cures, whereas 131I-MN-14 was still successful in 20%. Histol., no remaining viable tumor cells could be demonstrated in these animals surviving >6 mo. In patients, the MTD was reached at 60 mCi/m2 of hMN-14 (at 70 mCi/m2, two of three grade 4 myelotoxicities). Of 11 assessable patients, 2 had partial remissions (corresponding to an objective response rate of 18%), and 5 (45%) had minor/mixed responses or experienced stabilization of previously rapidly progressing disease. These data suggest that in small vol. disease, RAIT may be superior to conventional chemotherapy. Antibodies of higher affinity seem to be clearly superior. The clin. response rates in patients with small vol. disease are encouraging, being comparable to the response rates of conventional chemotherapeutic regimens but with fewer side effects. Ongoing studies will show whether ***treatment*** at the MTD will further improve ***therapeutic*** results.

REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L40 ANSWER 49 OF 76 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
 ACCESSION NUMBER: 1999342016 EMBASE
 TITLE: Novel agents for ***colorectal*** cancer.
 AUTHOR: Royce M.E.; Pazdur R.
 CORPORATE SOURCE: R. Pazdur, The University of Texas, MD Anderson Cancer
 Center, Division of Medicine, 1515 Holcombe Boulevard,
 Houston, TX 77030, United States. rpazdur@mdanderson.org
 SOURCE: Expert Opinion on Investigational Drugs, (1999) 8/10
 (1639-1652).
 Refs: 81
 ISSN: 1354-3784 CODEN: EOIDER
 COUNTRY: United Kingdom
 DOCUMENT TYPE: Journal; General Review
 FILE SEGMENT: 016 Cancer
 030 Pharmacology
 037 Drug Literature Index
 039 Pharmacy
 038 Adverse Reactions Titles
 048 Gastroenterology

LANGUAGE: English

SUMMARY LANGUAGE: English

AB The compound 5-fluorouracil (5-FU) has been investigated for over four decades; research has focussed on examining various schedules and biochemical modulators in an attempt to improve its ***therapeutic*** activity in advanced ***colorectal*** cancer. Combination chemotherapy regimens have not been developed because of the lack of other active agents. Recently, several novel agents are under clinical development for advanced ***colorectal*** cancer, including ***irinotecan***, oxaliplatin, oral fluoropyrimidines, raltitrexed, ***monoclonal*** antibody 17-1A and tumour vaccines. Both ***irinotecan*** and oxaliplatin have uniquely different mechanisms of action compared to 5-FU, and have demonstrated activity in patients whose disease has progressed with 5-FU ***treatment***. Recent randomised trials comparing 5-FU plus leucovorin (5-FU/LV) to combinations of either ***irinotecan*** or oxaliplatin plus 5-FU/LV, have demonstrated that the addition of these novel agents to 5-FU improve response rates (RRs) and time to progression (TTP). The role and acceptance of these combinations need to be defined, but are rapidly being introduced into the adjuvant ***therapy*** of ***colorectal*** cancer. Oral fluoropyrimidines (UFT plus leucovorin, capecitabine, eniluracil plus oral 5-FU, and S-1) provide the convenience of oral delivery with a marked reduction in febrile neutropenia and mucositis. To gain clinical acceptance, oral fluoropyrimidines must provide not only convenience and toxicity reduction, but also maintenance of survival advantages associated with optimal use of iv. 5-FU/LV regimens. These novel agents discussed herein provide ***treatment*** options which may allow for more individualised ***treatment*** strategies.

L40 ANSWER 50 OF 76 MEDLINE
 ACCESSION NUMBER: 1999356052 MEDLINE
 DOCUMENT NUMBER: 99356052 PubMed ID: 10425310
 TITLE: Synergistic growth inhibition and induction of apoptosis by a novel mixed backbone antisense oligonucleotide targeting CRIPTO in combination with C225 anti- ***EGFR*** ***monoclonal*** antibody and 8-Cl-cAMP in human GEO colon cancer cells.
 AUTHOR: Normanno N; Tortora G; De Luca A; Pomatito G; Casamassimi A; Agrawal S; Mendelsohn J; Bianco A R; Ciardiello F
 CORPORATE SOURCE: Oncologia Sperimentale D, ITN-Fondazione Pascale, 80131 Naples, Italy.
 SOURCE: ONCOLOGY REPORTS, (1999 Sep-Oct) 6 (5) 1105-9.
 Journal code: 9422756. ISSN: 1021-335X.
 PUB. COUNTRY: Greece
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals

ENTRY MONTH: 199908
 ENTRY DATE: Entered STN: 19990913
 Last Updated on STN: 19990913
 Entered Medline: 19990831

AB We have evaluated the antiproliferative effect of a novel mixed backbone antisense oligonucleotide generated against the 5'-coding region of the human CRIPTO mRNA in GEO human colon cancer cells. We have also evaluated the effects of this anti-CRIPTO antisense oligonucleotide in combination with a ***chimeric*** anti-human epidermal growth factor receptor (***EGFR***) ***monoclonal*** antibody (***MAB*** C225) and with 8-Cl-cAMP, a cAMP analog that specifically inhibits type I protein kinase A (PKAI), since a functional ***EGFR***-driven autocrine pathway is operative and PKAI is overexpressed in GEO colon cancer cells. ***Treatment*** with a single agent at low doses determined a 15-35% growth inhibition. A synergistic antiproliferative effect was observed when combinations of two agents were used with a co-operativity quotient ranging between 1.5 and 2.2. Furthermore, the combined ***treatment*** with all three drugs caused an almost complete suppression of the ability of GEO cells to form colonies in soft agar. We next evaluated whether any combination of 8-Cl-cAMP, the anti-CRIPTO antisense oligonucleotide and ***MAB*** C225 could induce programmed cell death in GEO cells. ***Treatment*** with each agent alone at all doses tested did not cause DNA fragmentation. The ***treatment*** with any combination of two agents was not able to induce apoptosis. In contrast, ***treatment*** with all three compounds determined an approximately three-fold increase in DNA fragmentation. In conclusion, the combination of selective antineoplastic agents directed against different but related key signal transduction pathways efficiently inhibits cell growth and causes apoptosis in human ***colorectal*** cancer cells.

L40 ANSWER 51 OF 76 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
 ACCESSION NUMBER: 1999400100 EMBASE

TITLE: Highlights of the 35th Annual Meeting of the American Society of Clinical Oncology.

AUTHOR: Prescott L.M.

SOURCE: P and T, (1999) 24/11 (553-554+556).

ISSN: 1052-1372 CODEN: PPTTEK

COUNTRY: United States

DOCUMENT TYPE: Journal; Conference Article

FILE SEGMENT: 006 Internal Medicine

016 Cancer

037 Drug Literature Index

038 Adverse Reactions Titles

LANGUAGE: English

L40 ANSWER 52 OF 76 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
 ACCESSION NUMBER: 1999164155 EMBASE

TITLE: Third International Conference on Biology, Prevention and ***Treatment*** of Gastrointestinal Malignancies.
 Cologne, 23-26 September 1998.

AUTHOR: Mayer R.J.

CORPORATE SOURCE: Dr. R.J. Mayer, Dana-Farber Cancer Institute, Harvard Medical School, 44 Binney Street, Boston, MA 02115, United States

SOURCE: Annals of Oncology, (1999) 10/3 (281-287).

ISSN: 0923-7534 CODEN: ANONE2

COUNTRY: Netherlands

DOCUMENT TYPE: Journal; Note

FILE SEGMENT: 006 Internal Medicine

016 Cancer

037 Drug Literature Index

038 Adverse Reactions Titles

048 Gastroenterology

LANGUAGE: English

SUMMARY LANGUAGE: English

AB R. Mayer (USA), summarizing the data presented during the three-day conference, stressed the importance of the development of new cytotoxic

drugs and - particularly - biological ***therapies*** as forms of ***treatment*** for patients with gastrointestinal malignancies. He also acknowledged the increasing application of molecular biology to gastrointestinal cancer through the identification of genetically-defined high-risk patients who merit costly screening techniques and the increased use of molecular 'markers' to serve as prognostic indicators and criteria for stratification in future clinical trials. Dr Mayer cautioned against allowing long-term frustration over poor surgical outcomes in patients with T3-4 esophageal cancer and enthusiasm derived from uncontrolled (i.e., phase II) trials to lead to the premature acceptance of preoperative chemoradiation ***therapy*** as standard ***treatment*** for such patients in the absence of properly controlled, adequately powered randomized studies. Dr Mayer reinforced the progress that has been made in the adjuvant ***treatment*** of colon cancer and noted the increasing number of new randomized studies that have been proposed to further enhance the likelihood for cure, particularly in patients with stage III disease. Dr Mayer concluded by presenting a series of hypothetical agenda items for the Fourth International Conference on Biology, Prevention, and ***Treatment*** of Gastrointestinal Malignancies to be held in the new millennium which he hoped would demonstrate the incorporation of biological agents into clinical trials, would document more concerted efforts to study the biology and improve the ***treatment*** for pancreatic cancer, and would begin to consider the use of 'risk-adapted' management strategies into clinical trials, based on such preclinical biological markers as intratumoral thymidylate synthase levels, apoptotic indices, allelic deletions, and the like.

L40 ANSWER 53 OF 76 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B. V.
 ACCESSION NUMBER: 1999390111 EMBASE
 TITLE: Adjuvant ***therapy*** of colon cancer.
 AUTHOR: Macdonald J.S.
 CORPORATE SOURCE: Prof. J.S. Macdonald, Department of Medicine, St. Vincents
 Comprehen. Cancer Ctr., New York, NY, United States
 SOURCE: Ca-A Cancer Journal for Clinicians, (1999) 49/4 (202-219).
 Refs: 59
 ISSN: 0007-9235 CODEN: CAMCAM
 COUNTRY: United States
 DOCUMENT TYPE: Journal; General Review
 FILE SEGMENT: 016 Cancer
 030 Pharmacology
 037 Drug Literature Index
 038 Adverse Reactions Titles
 048 Gastroenterology

LANGUAGE: English

SUMMARY LANGUAGE: English

AB Adjuvant ***therapy***, believed by some to be of no benefit for ***colorectal*** cancer as recently as 10 years ago, now offers thousands of patients considerable hope after surgical resection. The first effective adjuvant regimen - combined fluorouracil (5-FU) and levamisole - described in 1989, was soon supplanted by a variety of 5-FU-based regimens, usually combined with leucovorin. Although most recent research in the adjuvant setting has focused on refining chemotherapy doses, schedules, and combinations, with the aim of improving efficacy and decreasing toxicity, investigators have also explored other approaches, such as portal vein infusion, ***monoclonal*** antibodies, interferon-alpha, and vaccines. Future directions being evaluated for adjuvant ***therapy*** of colon cancer include the use of oral fluorinated pyrimidines, which may replace current intravenous ***treatments***, as well as the incorporation of new agents, such as oxaliplatin and CPT-11, into adjuvant chemotherapy programs.

L40 ANSWER 54 OF 76 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1998:534888 CAPLUS
 DOCUMENT NUMBER: 129:156926
 TITLE: Methods and compositions using receptor tyrosine
 kinase inhibitors for inhibiting cell proliferative
 disorders, and inhibitor preparation

INVENTOR(S): Chen, Hui; Gazit, Aviv; Hirth, Klaus Peter; Mann,
Elaina; Shawver, Laura K.; Tsai, Jianming; Tang, Peng
Cho
PATENT ASSIGNEE(S): Sugan, Inc., USA; Yisum Research & Development
Company of the Hebrew University of Jerusalem
SOURCE: U.S., 41 pp., Cont.-in-part of U.S. Ser. No. 207,933,
abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5789427	A	19980804	US 1995-399967	19950307
US 5773476	A	19980630	US 1995-486775	19950607
PRIORITY APPLN. INFO.:			US 1994-207933	19940307
			US 1995-399967	19950307

OTHER SOURCE(S): MARPAT 129:156926
AB The invention concerns compds. and their use to inhibit the activity of a
receptor tyrosine kinase. The invention is preferably used to
treat cell proliferative disorders, e.g. cancers characterized by
over-activity or inappropriate activity HER2 or ***EGFR***
REFERENCE COUNT: 90 THERE ARE 90 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L40 ANSWER 55 OF 76 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 1998254496 EMBASE
TITLE: [Cancerology: Search for optimal ***therapeutic***
schemes].
CANCEROLOGIE: A LA RECHERCHE DES MEILLEURS SCHEMAS
THERAPEUTIQUES
AUTHOR: Mabro M.
CORPORATE SOURCE: M. Mabro, Svc. de Medecine Interne-Oncologie, Hopital
Saint-Antoine, Paris, France
SOURCE: Presse Medicale, (11 Jul 1998) 27/24 (1228-1230).
ISSN: 0755-4982 CODEN: PRMEEM
COUNTRY: France
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 006 Internal Medicine
016 Cancer
026 Immunology, Serology and Transplantation
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: French

L40 ANSWER 56 OF 76 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 1999087983 EMBASE
TITLE: [Modern principles of combined ***treatment*** of
colon, rectal and anal canal cancers].
WSPOLCZESNE ZASADY LECZENIA SKOJARZONEGO RAKOW OKREZNICY,
ODBYTNICY I ODBYTU.
AUTHOR: Nowacki M.P.; Jaskola K.; Oledzki J.; Bujko K.; Siedlecki
P.
CORPORATE SOURCE: Dr. M.P. Nowacki, Klinika Chorob Jelita Grubego, Centrum
Onkologii-Instytut, ul. W.K. Roentgena 5, 02-781 Warszawa,
Poland
SOURCE: Nowotwory, (1998) 48/6 (1011-1030).
Refs: 86
ISSN: 0029-540X CODEN: NOWOAL
COUNTRY: Poland
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 016 Cancer
037 Drug Literature Index
048 Gastroenterology
LANGUAGE: Polish

SUMMARY LANGUAGE: English; Polish

AB The wide review of the literature has been carried out on the modern principles of ***treatment*** of the ***colorectal*** and anal canal cancers. The rationale, indications and the results of combined ***treatment*** - surgery and chemotherapy and/or radiotherapy is discussed. 5-fluorouracil modulated by the low doses of leucovorin administered intravenously in bolus is the standard regimen of the adjuvant chemotherapy, as well as palliative ***treatment*** in ***colorectal*** cancer patients. The efficacy of alternative routes of fluorouracil administration or its derivatives is currently still under investigation - mainly oral derivatives and various routes of administration: portal vein, intrarterial and intraperitoneal. Newer drugs such as ***irinotecan***, oxaliplatin, tomudex and ***monoclonal*** antibodies (Panorex) are under further clinical investigation. In rectal cancer patients, besides adjuvant chemotherapy, adjuvant radiotherapy is used, which as it was demonstrated by the recent randomised studies, prolongs survival. Traditional, standard postoperative radiotherapy is more frequently replaced by preoperative radiotherapy due to its higher efficacy, lower incidence of toxicity and higher probability of the sphincter-conserving surgery. In ***treatment*** of most patients with anal canal cancers the method of choice is radiochemotherapy. It ensures efficacy comparable to surgical ***treatment*** at the same time allowing for sphincter preservation.

L40 ANSWER 57 OF 76 MEDLINE

ACCESSION NUMBER: 1998418675 MEDLINE

DOCUMENT NUMBER: 98418675 PubMed ID: 9747879

TITLE: Nuclear targeting of Bax during apoptosis in human ***colorectal*** cancer cells.

AUTHOR: Mandal M; Adam L; Mendelsohn J; Kumar R

CORPORATE SOURCE: Department of Clinical Investigation, The University of Texas MD Anderson Cancer Center, Houston 77030, USA.

CONTRACT NUMBER: CA65746 (NCI)

SOURCE: ONCOGENE, (1998 Aug 27) 17 (8) 999-1007.

Journal code: 8711562. ISSN: 0950-9232.

PUB. COUNTRY: ENGLAND: United Kingdom

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199810

ENTRY DATE: Entered STN: 19981020

Last Updated on STN: 20000303

Entered Medline: 19981002

AB Homeostasis in colonic epithelial cells is regulated by the balance between proliferative activity and cell loss by apoptosis. Because epithelial cells at the apex of colonic crypts undergo apoptosis and proliferative activity is usually restricted to the base of the crypts, it has been proposed that the limited availability of growth factor-signals at the upper portions of the crypts may trigger apoptosis. In the present studies, we investigate the mechanism of apoptosis mediated by growth factor deprivation in ***colorectal*** carcinoma cells by delineating the possible involvement of Bax and its subcellular localization. We report that inhibition of epidermal growth factor receptor (***EGFR***) tyrosine kinase activity and downregulation of ***EGFR*** by anti-***EGFR*** ***mAb*** 225 induces apoptosis in human ***colorectal*** carcinoma DiFi and FET cells. Induction of apoptosis was preceded by enhanced expression of newly synthesized Bax protein, and required protein synthesis. In the ***mAb*** 225- ***treated*** cells, Bax was redistributed from the cytosol to the nucleus and subsequently, to the nuclear membranes. The observed induction of Bax expression by ***mAb*** 225 was not associated with p53 induction. However, ***mAb*** 225 ***treatment*** also triggered relocalization of p53 from the cytosol to a nuclear membrane-bound form. Induction of Bax and its redistribution to the nucleus of DiFi cells during apoptosis was also demonstrated in response to butyrate, a physiological relevant molecule in colonic epithelial cells as it is the principal short-chain fatty acid produced by bacterial fermentation of

dietary fiber in colonic epithelium. Using immunofluorescence and confocal microscopy, we observed that Bax is predominantly localized in the cytosol, but during apoptosis it is localized both inside and along the nuclear membrane. Taken together, these findings suggest that apoptosis induced by growth factor-deprivation or butyrate may involve the subcellular redistribution of Bax in human ***colorectal*** carcinoma cells.

L40 ANSWER 58 OF 76 MEDLINE
 ACCESSION NUMBER: 1998223363 MEDLINE
 DOCUMENT NUMBER: 98223363 PubMed ID: 9563874
 TITLE: Interactions between the epidermal growth factor receptor and type I protein kinase A: biological significance and ***therapeutic*** implications.
 AUTHOR: Ciardiello F; Tortora G
 CORPORATE SOURCE: Dipartimento di Endocrinologia e Oncologia Molecolare e Clinica, Facolta di Medicina e Chirurgia, Universita di Napoli Federico II, Italy.
 SOURCE: CLINICAL CANCER RESEARCH, (1998 Apr) 4 (4) 821-8. Ref: 78
 Journal code: 9502500. ISSN: 1078-0432.
 PUB. COUNTRY: United States
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 General Review; (REVIEW)
 (REVIEW, TUTORIAL)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 199805
 ENTRY DATE: Entered STN: 19980609
 Last Updated on STN: 20000303
 Entered Medline: 19980528

AB Peptide growth factors regulate normal cellular proliferation and differentiation through autocrine and paracrine pathways and are involved in cancer development and progression. Among the endogenous growth factors, the epidermal growth factor (EGF)-related proteins play an important role in the pathogenesis of human cancer. In fact, overexpression of EGF-related growth factors such as transforming growth factor alpha and amphiregulin and/or their specific receptor, the EGF receptor (***EGFR***), has been detected in several types of human cancers, including breast, lung, and ***colorectal*** cancers. Therefore, the blockade of ***EGFR*** activation by using anti-***EGFR*** ***monoclonal*** antibodies (MAbs) has been proposed as a potential anticancer ***therapy***. The cAMP-dependent protein kinase (PKA) is an intracellular enzyme with serine-threonine kinase activity that plays a key role in cell growth and differentiation. Two PKA isoforms with identical catalytic (C) subunits but different cAMP-binding regulatory (R) subunits (defined as RI in PKAI and RII in PKAII) have been identified. Predominant expression of PKAII is found in normal nonproliferating tissues and in growth-arrested cells, whereas enhanced levels of PKAI are detected steadily in tumor cells and transiently in normal cells exposed to mitogenic stimuli. Overexpression of PKAI has been correlated recently with poor prognosis in breast cancer patients. Inhibition of PKAI expression and function by specific pharmacological agents such as the selective cAMP analogue 8-chloro-cAMP (8-Cl-cAMP) induces growth inhibition in various human cancer cell lines in vitro and in vivo. We have provided experimental evidence of a functional cross-talk between ligand-induced ***EGFR*** activation and PKAI expression and function. In fact, PKAI is overexpressed and activated following transforming growth factor alpha-induced transformation in several rodent and human cell line models. Furthermore, PKAI is involved in the intracellular mitogenic signaling following ligand-induced ***EGFR*** activation. We have shown that an interaction between ***EGFR*** and PKAI occurs through direct binding of the RI subunit to the Grb2 adaptor protein. In this respect, PKAI seems to function downstream of the ***EGFR***, and experimental evidence suggests that PKAI is acting upstream of the mitogen-activated protein kinase pathway. We have also demonstrated that the functional interaction between the ***EGFR*** and the PKAI pathways could have potential ***therapeutic***

implications. In fact, the combined interference with both ***EGFR*** and PKA1 with specific pharmacological agents, such as anti- ***EGFR*** blocking MABs and cAMP analogues, has a cooperative antiproliferative effect on human cancer cell lines in vitro and in vivo. The antitumor activity of this combination could be explored in a clinical setting because both the 8-Cl-cAMP analogue and the anti- ***EGFR*** blocking ***MAB*** C225 have entered human clinical trial evaluation. Finally, both ***MAB*** C225 and 8-Cl-cAMP are specific inhibitors of intracellular mitogenic signaling that have different mechanisms of action compared with conventional cytotoxic drugs. In this respect, a cooperative growth-inhibitory effect in combination with several chemotherapeutic agents in a large series of human cancer cell lines in vitro and in vivo has been demonstrated for anti- ***EGFR*** blocking MABs or for 8-Cl-cAMP. Therefore, the combination of ***MAB*** C225 and 8-Cl-cAMP following chemotherapy could be investigated in cancer patients.

L40 ANSWER 59 OF 76 MEDLINE

ACCESSION NUMBER: 1998372662 MEDLINE

DOCUMENT NUMBER: 98372662 PubMed ID: 9708931

TITLE: New drugs in the ***treatment*** of ***colorectal*** carcinoma.

AUTHOR: Punt C J

CORPORATE SOURCE: Department of Medical Oncology, University Hospital Nijmegen, The Netherlands.

SOURCE: CANCER, (1998 Aug 15) 83 (4) 679-89. Ref: 115
Journal code: 0374236. ISSN: 0008-543X.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)

LANGUAGE: English

FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals

ENTRY MONTH: 199808

ENTRY DATE: Entered STN: 19980910

Last Updated on STN: 19980910

Entered Medline: 19980828

AB BACKGROUND: ***Treatment*** with 5-fluorouracil (5-FU) plus leucovorin has been the unofficial standard ***therapy*** for patients with ***colorectal*** carcinoma (CRC) for more than a decade; however, the optimal dose and schedule remain a matter of debate. Recently several new drugs have shown activity in this disease. These include ***irinotecan*** (CPT-11); oxaliplatin; the thymidylate synthase inhibitors raltitrexed, uracil/tegafur (UFT), capecitabine, and S-1; the biochemical modulators trimetrexate and 5-ethynyluracil; and the ***monoclonal*** antibody 17-1A. METHODS: The results of clinical trials with these and other new agents, as well as their current status and main characteristics, were reviewed. RESULTS: Several of these agents, some with a novel mechanism of action, show promising activity in CRC. In combination with 5-FU and leucovorin, trimetrexate showed encouraging response rates in Phase II studies. Other interesting agents include capecitabine, UFT, and S-1. The biochemical modulator 5-ethynyluracil may allow the oral administration of 5-FU; however, results of Phase II clinical trials are not yet available. CPT-11 is in the most advanced stage of development and, based on consistent data generated in extensive Phase II studies, currently appears to be a reasonable choice for 5-FU-resistant or refractory disease. Another promising agent is oxaliplatin, which showed activity as first-line and second-line ***treatment***. CONCLUSIONS: Several new agents have shown promise in the ***treatment*** of CRC, and changes in the standard ***treatment*** of advanced or high risk CRC appear likely in the near future.

L40 ANSWER 60 OF 76 MEDLINE

ACCESSION NUMBER: 1998300468 MEDLINE

DOCUMENT NUMBER: 98300468 PubMed ID: 9636839

TITLE: ***Irinotecan*** -induced immune thrombocytopenia.

AUTHOR: Bozec L; Bierling P; Fromont P; Levi F; Debat P; Cvitkovic

E; Misset J L
 CORPORATE SOURCE: FSMSIT, Hopital Paul Brousse, Villejuif, France.
 SOURCE: ANNALS OF ONCOLOGY, (1998 Apr) 9 (4) 453-5.
 Journal code: 9007735. ISSN: 0923-7534.
 PUB. COUNTRY: Netherlands
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 199809
 ENTRY DATE: Entered STN: 19980917
 Last Updated on STN: 19980917
 Entered Medline: 19980910
 AB BACKGROUND: ***Irinotecan*** is currently used as second-line chemotherapy for advanced ***colorectal*** cancer. We report a case of severe thrombocytopenia after ***Irinotecan***, suggesting an immune mechanism, in a 53-year-old patient. PATIENTS AND METHODS: The patient's sera were screened for platelet antibodies with an indirect platelet immunofluorescence test (PIIFT). The ***monoclonal*** antibody immobilization of platelet antigen assay (MAIPA) was used to characterize the antibody target. RESULTS: We detected an IgG platelet antibody in the patient's serum in the presence of ***Irinotecan*** by means of PIIFT, and not in the presence of SN-38, its active metabolite. The specificity of the binding was asserted after CD32 MoAb blockade. The platelet binding site could not be strictly identified with MAIPA and immunoblotting but GpIIb/IIIa can be excluded after experiments with Glanzmann platelets. CONCLUSION: This case can be considered the first documented ***Irinotecan***-induced immune thrombocytopenia.

L40 ANSWER 61 OF 76 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
 ACCESSION NUMBER: 1999414312 EMBASE
 TITLE: Multidisciplinary management of recurrent ***colorectal*** cancer.
 AUTHOR: Miller A.R.
 CORPORATE SOURCE: A.R. Miller, Department of Surgery, University of Texas, Health Science Center at San Antonio, 7703 Floyd Curl Drive, San Antonio, TX 78248, United States.
 millerar@uthscsa.edu
 SOURCE: Surgical Oncology, (1998) 7/3-4 (209-221).
 Refs: 118
 ISSN: 0960-7404 CODEN: SUOCEC
 PUBLISHER IDENT.: S 0960-7404(99)00019-5
 COUNTRY: United Kingdom
 DOCUMENT TYPE: Journal; General Review
 FILE SEGMENT: 001 Anatomy, Anthropology, Embryology and Histology
 014 Radiology
 016 Cancer
 023 Nuclear Medicine
 026 Immunology, Serology and Transplantation
 030 Pharmacology
 037 Drug Literature Index
 048 Gastroenterology
 009 Surgery
 LANGUAGE: English
 SUMMARY LANGUAGE: English

AB Isolated pelvic recurrence of rectal carcinoma may occur in up to one third of patients following definitive resection of primary disease. The means by which recurrence is diagnosed, methods by which it may be ***treated***, and reported outcomes are all evolving and improving. Current data indicate that a substantial proportion of patients ***treated*** by aggressive multi-modality salvage ***therapy*** may be provided with durable survival. This review highlights current concepts in the diagnosis and management of locally recurrent rectal carcinoma.
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L40 ANSWER 62 OF 76 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
 ACCESSION NUMBER: 1998219764 EMBASE
 TITLE: Flood of new research brings hope to many cancer patients.

AUTHOR: Portyansky E.
 SOURCE: Drug Topics, (15 Jun 1998) 142/12 (37).
 ISSN: 0012-6616 CODEN: DGTNA7
 COUNTRY: United States
 DOCUMENT TYPE: Journal; (Short Survey)
 FILE SEGMENT: 016 Cancer
 030 Pharmacology
 037 Drug Literature Index
 LANGUAGE: English

L40 ANSWER 63 OF 76 MEDLINE

ACCESSION NUMBER: 1998150752 MEDLINE

DOCUMENT NUMBER: 98150752 PubMed ID: 9491788

TITLE: Continuing the fight against advanced ***colorectal***
 cancer: new and future ***treatment*** options.

AUTHOR: Bleiberg H

CORPORATE SOURCE: Chemotherapy and Gastroenterology Unit, Institut Jules
 Bordet, Universite Libre de Bruxelles, Brussels, Belgium.

SOURCE: ANTI-CANCER DRUGS, (1998 Jan) 9 (1) 18-28. Ref: 83
 Journal code: 9100823. ISSN: 0959-4973.

PUB. COUNTRY: ENGLAND: United Kingdom

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 General Review; (REVIEW)
 (REVIEW, TUTORIAL)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199804

ENTRY DATE: Entered STN: 19980430
 Last Updated on STN: 19980430
 Entered Medline: 19980417

AB The benefit of chemotherapy in the ***treatment*** of advanced
 colorectal cancer has now been clearly demonstrated with several
 studies reporting advantages in terms of overall survival, quality of life
 and effective palliation following chemotherapy plus supportive care in
 comparison to supportive care alone. However, the survival benefit
 achieved with the current 5-fluorouracil (5-FU)-based regimens is modest
 and thus investigations are ongoing to identify more effective agents with
 novel mechanisms of action. The three new agents likely to have the
 greatest impact in the near future are the thymidylate synthase inhibitor
 ZD1694 (Tomudex), the topoisomerase I inhibitor ***irinotecan***
 (Campto) and the new platinum compound, oxaliplatin (L-OHP). Promising
 response rates of 26 and 20% have been reported with ZD1694 in patients
 with advanced ***colorectal*** cancer in phase II and III studies,
 respectively. In a European phase II study, ***irinotecan*** has
 achieved response rates of 19% in chemotherapy-naïve patients and 18% in
 pretreated patients with advanced disease. Oxaliplatin has mainly been
 investigated in combination with continuous infusion 5-FU, with response
 rates of 29-58%. Other agents currently in development include
 monoclonal antibodies (e.g. 17-1A and MN-14), protein synthesis
 inhibitors (e.g. RA 700) and angiogenesis inhibitors (e.g. PF 4).

L40 ANSWER 64 OF 76 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.

ACCESSION NUMBER: 97298899 EMBASE

DOCUMENT NUMBER: 1997298899

TITLE: [Current aspects of adjuvant and palliative chemotherapy in
 colorectal carcinoma].

AKTUELLE ASPEKTE ZUR ADJUVANTEN UND PALLIATIVEN
 CHEMOTHERAPIE BEIM KOLOREKTALEN KARZINOM.

AUTHOR: Bokemeyer C.; Hartmann J.T.; Kanz L.

CORPORATE SOURCE: C. Bokemeyer, Eberhard-Karls-Universitat, Abteilung Innere
 Medizin II, Hamatologie und Onkologie, Otfried-Muller-
 Strasse 10, D-72076 Tubingen, Germany

SOURCE: Schweizerische Rundschau fur Medizin/Praxis, (1997) 86/39
 (1510-1516).
 Refs: 11

ISSN: 0369-8394 CODEN: SRMPDJ

COUNTRY: Switzerland

DOCUMENT TYPE: Journal; (Short Survey)

FILE SEGMENT: 016 Cancer

026 Immunology, Serology and Transplantation

048 Gastroenterology

037 Drug Literature Index

LANGUAGE: German

SUMMARY LANGUAGE: English; German

AB With an annual incidence rate of 30 to 40 per 100,000 ***colorectal*** carcinoma is the second most frequent malignancy in Germany. Despite the poor outcome of patients suffering from this disease important advances have been made in the standardisation and improvement of palliative and adjuvant ***treatment*** in patients with ***colorectal*** cancer. For the systemic chemotherapy 5-fluorouracil (5-FU) remains the most important cytotoxic agent and biomodulation of the ***therapeutic*** activity of 5-FU with methotrexate or particularly folinic acid has been clinically established, yielding response rates of 20 to 35% of patients. Current investigations of systemic ***treatment*** are aiming into three directions; 1. investigation of high-dose continuous (24-hours) 5-FU application (with or without modulation by folinic acid); 2. evaluation of new, effective cytotoxic agents, among which the camptotecin derivative CPT-11 (irinotecan) and the specific thymidilate synthase inhibitor Tomudex appear to be the most promising drugs as single agents and/or in combination with 5-FU; 3. use of orally available fluoropyrimidine derivatives with high bioavailability which may substantially improve the quality of life in palliative ***therapy***. The postoperative adjuvant ***treatment*** of patients with Dukes C ***colorectal*** cancer is established clinical practice and the combination of 5-FU and levamisole given for one year will result in an improved overall survival of about 15% at five years compared to surgery alone. Although this regimen remains the current standard ***treatment***, alternatives for the adjuvant ***treatment*** may be the use of 5-FU and folinic acid given for only half a year post surgery, locoregional perfusion of the liver with 5-FU alone via the portal vein by 7-day continuous application or the use of 17-1A ***monoclonal*** antibody immunotherapy after curative resection. Further improvement may be achieved by the combination of immunotherapy and chemotherapy which is currently tested in clinical studies. Future recommendations for the adjuvant ***treatment*** of ***colorectal*** cancer will not only be based on ***therapeutic*** efficacy but will also have to take costs of ***treatment*** into account. Better definition of high-risk patient groups for adjuvant ***treatment*** is needed.

L40 ANSWER 65 OF 76 MEDLINE

ACCESSION NUMBER: 1999111058 MEDLINE

DOCUMENT NUMBER: 99111058 PubMed ID: 9815809

TITLE: Clinical and immune responses in advanced
colorectal cancer patients ***treated*** with
anti-idiotypic ***monoclonal*** antibody vaccine that
mimics the carcinoembryonic antigen.

AUTHOR: Foon K A; John W J; Chakraborty M; Sherratt A; Garrison J;
Flett M; Bhattacharya-Chatterjee M

CORPORATE SOURCE: Lucille Parker Markey Cancer Center, Department of Internal
Medicine, Division of Hematology/Oncology, University of
Kentucky Medical Center, Lexington, Kentucky 40536, USA.

CONTRACT NUMBER: PO1 CA5880-01 (NCI)

SOURCE: CLINICAL CANCER RESEARCH, (1997 Aug) 3 (8) 1267-76.

Journal code: 9502500. ISSN: 1078-0432.

PUB. COUNTRY: United States

DOCUMENT TYPE: (CLINICAL TRIAL)

Journal; Article; (JOURNAL ARTICLE)

(RANDOMIZED CONTROLLED TRIAL)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199902

ENTRY DATE: Entered STN: 19990311

Last Updated on STN: 19990311

Entered Medline: 19990225

AB Carcinoembryonic antigen (CEA) is expressed in a wide variety of adenocarcinomas, and it is well recognized that cancer patients are immunologically "tolerant" to CEA. The purpose of this study was to determine whether we could break immune tolerance to CEA by vaccinating patients with a ***monoclonal*** anti-idiotypic antibody that is the internal image of CEA and to determine what impact this might have on patient survival. Twenty-four patients with advanced CEA-positive ***colorectal*** cancer who failed standard ***therapies*** except for two were entered into this Phase Ib trial. One patient was considered not assessable, because on the day of entering into the study, she was diagnosed with acute myelogenous leukemia. Patients were ***treated*** with 1, 2, or 4 mg of aluminum hydroxide-precipitated 3H1 anti-idiotypic antibody every other week for four injections and then monthly until tumor progression was observed. Immunological monitoring included humoral and cellular idiotypic and CEA responses, and all patients were evaluated for toxicity, response, and survival. Hyperimmune sera from 17 of 23 patients demonstrated an anti-anti-idiotypic Ab3 response, and 13 of these responses were demonstrated to be true anti-CEA responses (Ab1'). The antibody response was polyclonal, and 11 mediated antibody-dependent cellular cytotoxicity. Ten patients had idiotypic T-cell responses, and five had specific T-cell responses to CEA. None of the patients had objective clinical responses, but overall median survival for the 23 evaluable patients was 11.3 months, with 44% 1-year survival (95% confidence interval, 23-64%). Toxicity was limited to local swelling and minimal pain. Anti-idiotypic ***monoclonal*** antibody 3H1 that mimics CEA was able to break immune tolerance in the majority of ***treated*** patients. Overall survival of 11.3 months was comparable to other phase II data with advanced ***colorectal*** cancer patients ***treated*** with a variety of chemotherapy agents, including ***irinotecan***, with considerably less toxicity. Although it is not clear that the vaccine itself had an impact on survival, this should be determined in a Phase III randomized trial.

L40 ANSWER 66 OF 76 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.

ACCESSION NUMBER: 97233830 EMBASE

DOCUMENT NUMBER: 1997233830

TITLE: The role of adjuvant chemotherapy in the ***treatment*** of ***colorectal*** cancer.

AUTHOR: Vaughn D.J.; Haller D.G.

CORPORATE SOURCE: Dr. D.J. Vaughn, Hematology/Oncology Division, Univ. of Pennsylvania Cancer Center, 6 Penn Tower, 3400 Spruce Street, Philadelphia, PA 19104-6100, United States

SOURCE: Hematology/Oncology Clinics of North America, (1997) 11/4 (699-719).

Refs: 92

ISSN: 0889-8588 CODEN: HCNAEQ

COUNTRY: United States

DOCUMENT TYPE: Journal; General Review

FILE SEGMENT: 016 Cancer

037 Drug Literature Index

038 Adverse Reactions Titles

048 Gastroenterology

LANGUAGE: English

SUMMARY LANGUAGE: English

AB Adjuvant ***therapy*** is clearly of great benefit for certain patients with ***colorectal*** carcinoma. Validation of new prognostic markers to further define which patients are at highest risk of recurrence will be important. Future investigation for adjuvant ***therapy*** includes incorporation of achievements made in the advanced disease setting, including biochemical modulation of 5-FU, identification of new active agents, and incorporation of immunotherapy strategies into adjuvant ***treatment*** programs. Further improvements in the ***treatment*** of these patients, even if small, may translate into important benefits, given the large number of patients presenting annually with this common cancer. As our ***therapeutic*** options broaden and improve, investigators will need to focus on quality of life and pharmacoeconomic parameters to determine which adjuvant approaches are optimal for the

individual patient with ***colorectal*** cancer, as well as for society in general.

L40 ANSWER 67 OF 76 MEDLINE
 ACCESSION NUMBER: 97253219 MEDLINE
 DOCUMENT NUMBER: 97253219 PubMed ID: 9098662
 TITLE: ***Treatment*** of ***colorectal*** cancer. Current guidelines and future prospects for drug ***therapy***.
 COMMENT: Erratum in: Drugs 1997 Jul;54(1):160
 AUTHOR: Labianca R; Pessi M A; Zamparelli G
 CORPORATE SOURCE: Division of Medical Oncology, S. Carlo Borromeo Hospital, Milan, Italy.
 SOURCE: DRUGS, (1997 Apr) 53 (4) 593-607. Ref: 89
 Journal code: 7600076. ISSN: 0012-6667.
 PUB. COUNTRY: New Zealand
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 General Review; (REVIEW)
 (REVIEW, TUTORIAL)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 199706
 ENTRY DATE: Entered STN: 19970716
 Last Updated on STN: 19990129
 Entered Medline: 19970630

AB ***Colorectal*** carcinoma is one of the most common cancers in Western countries (yearly incidence rate of 1:3000), and represents, after lung cancer, the second leading cause of deaths due to cancer. During the past decades, knowledge about this carcinoma has considerably increased, but little progress has been made in improvement in patient survival. At least 40% of patients with ***colorectal*** cancer will have metastases sometime during the course of their illness. In colon cancer, the first ***therapeutic*** approach is surgery, but the important role of adjuvant chemotherapy in these patients, in terms of disease-free survival and overall survival benefit, is now well established. Until today, standard ***therapy*** was represented by fluorouracil plus levamisole and/or calcium folinate (folinic acid). Other strategies are represented by ***monoclonal*** antibodies (***mAb***), which improve survival, (with a decrease in mortality by 32%), and by portal vein fluorouracil, alone or in combination with systemic ***therapy***. In rectal cancer, the best results have been obtained with a combination of radiotherapy and chemotherapy. In advanced ***colorectal*** cancer, a standard ***treatment*** has not yet been established. This disease is usually considered as poorly chemosensitive and for more than 30 years fluorouracil has been the standard drug. Tumour response rates (partial+complete) for patients ***treated*** with bolus intravenous fluorouracil are 10 to 15%, with a median survival about 1 year. Many attempts have been made to improve these results. Biochemical modulation of fluorouracil is one of the most interesting strategies developed in the last few years in an attempt to increase the ***therapeutic*** index of this compound. Another way has been to administer fluorouracil by continuous infusion. Further innovative compounds such as ***irinotecan*** and raltitrexed are now being evaluated in clinical trials. Preliminary data from phase II and III studies have provided encouraging results on the use of these new drugs. In metastatic disease confined to the liver, the possibility of locoregional ***therapy*** through implantable pumps should be taken into consideration.

L40 ANSWER 68 OF 76 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
 ACCESSION NUMBER: 1997:298615 BIOSIS
 DOCUMENT NUMBER: PREV199799597818
 TITLE: ***Colorectal*** cancer - Is there an alternative to 5-FU.
 AUTHOR(S): Bleiberg, H.
 CORPORATE SOURCE: Chemother. Gastroenterol. Unit, Inst. Jules Bordet, Univ. Libre de Bruxelles, Rue Heger Bordet, B-1000 Brussels
 Belgium
 SOURCE: European Journal of Cancer, (1997) Vol. 33, No. 4, pp.

536-541.

ISSN: 0959-8049.

DOCUMENT TYPE: General Review

LANGUAGE: English

L40 ANSWER 69 OF 76 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.

ACCESSION NUMBER: 97070124 EMBASE

DOCUMENT NUMBER: 1997070124

TITLE: Adjuvant medical ***therapy*** for ***colorectal*** cancer.

AUTHOR: Diaz-Canton E.A.; Pazdur R.

CORPORATE SOURCE: Dr. R. Pazdur, Division of Medicine, U.T.M.D. Anderson Cancer Center, Box 92, 1515 Holcombe Boulevard, Houston, TX 77030, United States

SOURCE: Surgical Clinics of North America, (1997) 77/1 (211-228).

Refs: 67

ISSN: 0039-6109 CODEN: SCNA7

COUNTRY: United States

DOCUMENT TYPE: Journal; General Review

FILE SEGMENT: 009 Surgery

016 Cancer

037 Drug Literature Index

038 Adverse Reactions Titles

LANGUAGE: English

SUMMARY LANGUAGE: English

AB In the mid-1980s, trials of adjuvant ***therapy*** for colon cancer in the United States had a 'no ***treatment***' arm, which reflected the belief that effective adjuvant chemotherapy did not exist for patients with surgically resected disease at high risk for recurrence. However, with the observation in the early 1990s that postsurgical adjuvant 5-FU plus levamisole reduced tumor recurrence and ultimately increased overall survival in stage III colon cancer, the potential of effective adjuvant chemotherapy was realized. Questions about the duration of adjuvant chemotherapy, the specifics of chemotherapy schedule/drug selection, and its use in stage II colon cancer are beginning to be clarified in large, randomized adjuvant ***therapy*** trials. In rectal carcinomas, combined modality postoperative pelvic irradiation plus chemotherapy for stage II and III disease has been shown to reduce both local and systemic recurrences and to prolong survival compared with that in patients ***treated*** with local surgery and radiation. Again, large randomized trials are attempting to clarify both the optimal chemotherapeutic agents and schedules to be used and also whether preoperative combined modality ***therapy*** can improve the resectability rate, rate of sphincter preservation, and survival. Future trials will examine new agents shown to be effective in advanced disease as well as ***monoclonal*** antibodies, such as MoAb 17-1A, that may have selective activity in minimal disease. Improvement in overall survival remains the ultimate endpoint of future adjuvant ***therapy*** trials; however, trials will also critically examine toxicity, quality of life, pharmacoeconomics, and genetic and biologic correlates that may help select more appropriate candidates for adjuvant ***therapies***.

L40 ANSWER 70 OF 76 MEDLINE

ACCESSION NUMBER: 1998098165 MEDLINE

DOCUMENT NUMBER: 98098165 PubMed ID: 9435876

TITLE: Clinical experience with CD64-directed immunotherapy. An overview.

AUTHOR: Curnow R T

CORPORATE SOURCE: Medarex Inc., Annadale, NJ 08801, USA.

SOURCE: CANCER IMMUNOLOGY, IMMUNOTHERAPY, (1997 Nov-Dec) 45 (3-4) 210-5. Ref: 9

Journal code: 8605732. ISSN: 0340-7004.

PUB. COUNTRY: GERMANY: Germany, Federal Republic of

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

General Review; (REVIEW)

(REVIEW LITERATURE)

LANGUAGE: English

09/04, 921

FILE SEGMENT: Priority Journals
 ENTRY MONTH: 199801
 ENTRY DATE: Entered STN: 19980206
 Last Updated on STN: 20000303
 Entered Medline: 19980129

AB The class I IgG receptor (Fc gamma RI or CD64 receptor), which is present on key cytotoxic effector cells, has been shown to initiate the destruction of tumor cells in vitro and has been hypothesized to play a role in the destruction of antibody-coated cells such as platelets in idiopathic thrombocytopenia purpura (ITP). This overview summarizes the clinical experience with CD64-directed immunotherapy in cancer patients with the bispecific antibodies MDX-447 [***humanized*** Fab anti-CD64 x ***humanized*** Fab anti-(epidermal growth factor receptor, ***EGFR***)] and MDX-H210 (***humanized*** Fab anti-DC64 x Fab anti-HER2/neu), and with the anti-CD64 ***monoclonal*** antibody (***mAB***) MDX-33 (H22) in the modulation of monocyte CD64 in vivo. In an ongoing phase I/II open-label trial with progressive dose escalation (1-15 mg/m2), patients with ***treatment*** refractory ***EGFR*** -positive cancers (renal cell carcinoma (RCC), head and neck, bladder, ovarian, prostate cancer and skin cancer) are ***treated*** weekly with intravenous MDX-447, with and without granulocyte-colony-stimulating factor (G-CSF). MDX-447 has been found to be immunologically active at all doses, binding to circulating monocytes and neutrophils (when given with G-CSF), causing monocytopenia and stimulating increases in circulating plasma cytokines. MDX-447 is well tolerated, the primary toxicities being fever, chills, blood pressure lability, and pain/ myalgias. Of 36 patients evaluable for response, 9 have experienced stable disease of 3-6 month's duration. The optimal dose and the maximal tolerated dose (MTD) have yet to be defined; dose escalation continues to define better the dose, toxicity, and the potential ***therapeutic*** role of this bispecific antibody. Three MDX-H210 phase II trials are currently in progress, all using the intravenous dose of 15 mg/m2 given with granulocyte/macrophage (GM-CSF). These consist of one trial each in the ***treatment*** of RCC patients, patients with prostate cancer, and ***colorectal*** cancer patients, all of whom have failed standard ***therapy***. At the time of writing, 11 patients have been ***treated*** in these phase II trials. Four patients have demonstrated antitumor effects. Patients demonstrating responses include 2 with RCC and 2 with prostate cancer. One RCC patient has had a 54% reduction in size of a hepatic metastatic lesion and the other has had a 49% decrease in the size of a lung metastasis with simultaneous clearing of other non-measurable lung lesions. Regarding the two patients with prostate cancer, one has had a 90% reduction in serum prostate-specific antigen (PSA; 118-11 ng/ml), which has persisted for several months; the other patient with prostate has had a 70% reduction of serum PSA (872 ng/ml to 208 ng/ml) within the first month of ***treatment***. Both patients have also demonstrated symptomatic improvement. In a completed phase I and in ongoing phase I/II clinical trials, patients with ***treatment*** -refractory HER2/neu positive cancers (breast, ovarian, ***colorectal***, prostate) have been ***treated*** with MDX-H210, which has been given alone and in conjunction with G-CSF, GM-CSF, and interferon gamma (IFN gamma). These trials have been open-label, progressive dose-escalation (0.35-135 mg/m2) studies in which single, and more often, multiple weekly doses have been administered. MDX-H210 has been well tolerated, with untoward effects being primarily mild-to-moderate flu-like symptoms. The MTD has not yet been defined. MDX-H210 is immunologically active, binding to circulating monocytes, causing monocytopenia, as well as stimulating increases in plasma cytokine levels. Furthermore, some patients have evidence of active antitumor immunity following ***treatment*** with MDX-210. Antitumor effects have been seen in response to MDX-H210 administration; these include 1 partial, 2 minor, and 1 mixed tumor response; 15 protocol-defined stable disease responses have occurred. (ABSTRACT TRUNCATED)

L40 ANSWER 71 OF 76 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
 ACCESSION NUMBER: 97116392 EMBASE
 DOCUMENT NUMBER: 1997116392

TITLE: Summary of the epidemiological situation concerning malignancies in the province of Vojvodina in the period 1985 to 1994.
 AUTHOR: Mikov M.; Vranjes N.
 SOURCE: Archive of Oncology, (1997) 5/1 (33-34).
 ISSN: 0354-2351 CODEN: ARONFV
 COUNTRY: Yugoslavia
 DOCUMENT TYPE: Journal; Note
 FILE SEGMENT: 016 Cancer
 017 Public Health, Social Medicine and Epidemiology
 037 Drug Literature Index
 LANGUAGE: English

L40 ANSWER 72 OF 76 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
 ACCESSION NUMBER: 97243403 EMBASE
 DOCUMENT NUMBER: 1997243403

TITLE: [First line chemotherapy for advanced ***colorectal*** cancers].
 CHIMIOThERAPIE DE PREMIERE INTENTION DES CANCERS COLO-RECTAUX EVOLUES.
 AUTHOR: Becouarn Y.
 CORPORATE SOURCE: Y. Becouarn, Service d'oncologie digestive, Institut Bergonie, Ctr. regional lutte contre cancer, 180, rue de Saint-Genes, 33076 Bordeaux cedex, France
 SOURCE: Revue du Praticien, (1997) 47/12 SUPPL. (22-28).
 Refs: 24
 ISSN: 0035-2640 CODEN: REPRA3
 COUNTRY: France
 DOCUMENT TYPE: Journal; (Short Survey)
 FILE SEGMENT: 016 Cancer
 030 Pharmacology
 037 Drug Literature Index
 038 Adverse Reactions Titles
 048 Gastroenterology
 LANGUAGE: French

SUMMARY LANGUAGE: English; French

AB Neatly six patients out of ten have or will have ***colorectal*** metastasis. A first line chemotherapy is justified as patients' survival duration, quality of life and life without symptoms will be longer and as antitumor efficacy is real. Among classical 5-FU based intravenous chemotherapies the 5-FU plus folinic acid combination should be preferred to the 5-FU plus methotrexate combination, the latter being difficult to survey. If continuous 5-FU infusions induce more response than 5-FU bolus alone, they are similar to 5-FU bolus plus folinic acid, but more expensive to realise. Practically, the french chemotherapy protocol that we recommend in first line is a combination of bi-weekly 5-FU bolus plus continuous 5-FU infusion plus folinic acid, which has more efficacy and which is really less toxic than other 5-FU modulations. Among the new drugs available, raltitrexed is the only one authorized by the French government in first line ***therapy***. Other ***therapeutic*** ways are possible as hepatic intra-arterial chemotherapy (for some special cases). The future consists of pursuing trials to evaluate chronomodulated chemotherapy, individual adjustment of 5-FU dose, and new drugs.

L40 ANSWER 73 OF 76 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
 ACCESSION NUMBER: 1998018581 EMBASE

TITLE: Perspectives on new chemotherapeutic agents in the ***treatment*** of colo rectal cancer.
 AUTHOR: Clark J.W.
 CORPORATE SOURCE: Dr. J.W. Clark, Massachusetts General Hospital, Dept. of Hematology/Oncology, Cox, 100 Blossom St, Boston, MA 02114, United States
 SOURCE: Seminars in Oncology, (1997) 24/5 SUPPL. 18 (S18-19-S18-24).
 Refs: 54
 ISSN: 0093-7754 CODEN: SOLGAV
 COUNTRY: United States

DOCUMENT TYPE: Journal; General Review

FILE SEGMENT: 016 Cancer

030 Pharmacology

037 Drug Literature Index

038 Adverse Reactions Titles

048 Gastroenterology

LANGUAGE: English

SUMMARY LANGUAGE: English

AB In patients with metastatic ***colorectal*** cancer (CRC), conventional chemotherapy with 5-fluorouracil (5-FU) plus leucovorin provides an overall response rate of approximately 25% but has had little effect on survival. Thus, alternate agents, new combinations of agents, and new ***treatment*** strategies are being investigated. Research efforts over the past decade have increased our understanding of how anticancer agents mediate their antitumor effects, and specific targets for inhibiting the survival, growth, or metastasis of CRC cells have been elucidated. Advances in our understanding have led not only to improvements in the application of currently available agents, but also to the discovery of new agents with activity in CRC. The following active areas of research and/or ***treatment*** approaches are discussed: (1) approaches for enhancing 5-FU/leucovorin activity; (2) novel delivery of 5-FU or 5-FU precursor agents; (3) new thymidylate synthase inhibitors; (4) new platinum analogues; (5) topoisomerase I inhibitors; (6) targeting specific proteins or pathways important for the growth, survival, or metastasis of CRC cells; (7) biologic response modifiers, including ***monoclonal*** antibodies; and (8) gene ***therapy***. As the cellular mechanisms involved in CRC are further defined and chemotherapy or biologic agents more precisely targeted, response rates and ultimately survival will hopefully improve in this patient population.

L40 ANSWER 74 OF 76 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.

ACCESSION NUMBER: 96041618 EMBASE

DOCUMENT NUMBER: 1996041618

TITLE: New concepts for the development and use of antifolates.

AUTHOR: Chu E.; Grem J.L.; Johnston P.G.; Allegra C.J.

CORPORATE SOURCE: NCI-Navy Medical Oncology Branch, National Cancer Institute, National Institutes of Health, 8901 Wisconsin Avenue, Bethesda, MD 20889-5105, United States

SOURCE: Stem Cells, (1996) 14/1 (41-46).

ISSN: 1066-5099 CODEN: STCEEJ

COUNTRY: United States

DOCUMENT TYPE: Journal; General Review

FILE SEGMENT: 016 Cancer

029 Clinical Biochemistry

030 Pharmacology

037 Drug Literature Index

038 Adverse Reactions Titles

LANGUAGE: English

SUMMARY LANGUAGE: English

AB Approximately one-third of all cases of ***colorectal*** carcinoma present in an advanced and, therefore, incurable stage. For these patients, the development of new chemotherapeutic strategies is of central importance. Biochemical modulation of 5-fluorouracil (5-FU) has resulted in approximately a two-fold increase in activity of 5-FU. Recent preclinical investigations suggest that interferon can also modulate the activity of 5-FU and may result in enhanced response rates in patients. One of the critical mechanisms of resistance to 5-FU appears to be the acute induction in thymidylate synthase (TS) levels following ***therapy*** with inhibitors of this enzyme. This mechanism is based on a novel autoregulatory feedback pathway wherein the TS protein regulates its own translational efficiency. Regulatory function of the enzyme is dependent on its state of occupancy by either the physiologic ligands or inhibitors, including flouropirimidines and antifolates. Ongoing efforts are directed towards utilizing knowledge of this protein/messenger RNA interaction for ***therapeutic*** benefit. Given the importance of TS, our laboratory has developed antibodies capable of quantitating the levels of this enzyme in fresh or paraffin-embedded tissues. Preliminary

investigations suggest that the level of TS has prognostic importance in patients with rectal carcinoma and may be used to predict responsiveness to fluoropyrimidine agents. Novel strategies utilizing dual modulation of 5-FU with leucovorin and interferon are under investigation in both the advanced and adjuvant disease settings. Emerging mechanistic concepts regarding TS, along with the development of new, more potent inhibitors will hopefully result in future ***therapeutic*** gains.

L40 ANSWER 75 OF 76 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
 ACCESSION NUMBER: 95260259 EMBASE
 DOCUMENT NUMBER: 1995260259
 TITLE: An overview of adjuvant ***therapy*** for
 colorectal cancer.
 AUTHOR: Haller D.G.
 CORPORATE SOURCE: Hematology-Oncology Division, Hospital of the Univ.of
 Pennsylvania, University of Pennsylvania Med. Ctr, 3400
 Spruce Street, Philadelphia, PA 19104, United States
 SOURCE: European Journal of Cancer Part A: General Topics, (1995)
 31/7-8 (1255-1263).
 ISSN: 0959-8049 CODEN: EJCTEA
 COUNTRY: United Kingdom
 DOCUMENT TYPE: Journal; General Review
 FILE SEGMENT: 009 Surgery
 016 Cancer
 048 Gastroenterology
 037 Drug Literature Index

LANGUAGE: English

SUMMARY LANGUAGE: English

AB Adjuvant ***therapy*** of ***colorectal*** cancer is one of the most active areas of clinical oncology research. Although the data for the benefits from early trials of adjuvant ***therapy*** were inconclusive, these trials suffered from inadequate sample sizes, poor staging, potentially suboptimal ***treatment*** regimens and ill-defined prognostic subgroups. More recently, larger trials of higher scientific quality have demonstrated that regimens of fluorouracil plus levamisole in stage III colon cancer and fluorouracil with postoperative radiation in stages II and III rectal cancer can reduce mortality. Such regimens have now become standard practice in settings in which ***treatment*** is believed to be both efficacious and tolerable, and when the overall impact of ***therapy*** is considered to be clinically relevant. More recent advances in adjuvant ***treatment*** of ***colorectal*** cancer further support the role of fluorouracil-based regimens. Peri-operative portal vein infusions of fluorouracil demonstrate improved relapse-free and overall survival, and infusional fluorouracil administered with radiation for rectal primaries appears superior to less intensive bolus fluorouracil regimens. Completed trials of fluorouracil plus leucovorin combinations are awaiting maturation, with expectations for superior adjuvant activity based on demonstrated improved response rates for biochemically modulated fluorouracil in advanced metastatic ***colorectal*** cancer. New systemic agents are also entering large-scale adjuvant trials, including ***monoclonal*** antibody 17-1a, given alone and in conjunction with standard fluorouracil regimens. Additional cytotoxic drugs, including CPT-11 and Tomudex, offer new opportunities for alternative adjuvant regimens for the large, heterogeneous population of patients with resected ***colorectal*** cancer.

L40 ANSWER 76 OF 76 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
 ACCESSION NUMBER: 94051228 EMBASE
 DOCUMENT NUMBER: 1994051228
 TITLE: Indium-111-labeled anti- ***EGFr*** -425 scintigraphy in
 the detection of malignant gliomas.
 AUTHOR: Dadparvar S.; Krishna L.; Miyamoto C.; Brady L.W.; Brown
 S.J.; Bender H.; Slizofski W.J.; Eshleman J.; Chevres A.;
 Woo D.V.
 CORPORATE SOURCE: Nuclear Medicine, Hahnemann University, Broad and Vine
 Streets, Philadelphia, PA 19102-1192, United States

SOURCE: Cancer, (1994) 73/SUPPL. (884-889).
 ISSN: 0008-543X CODEN: CANCAR
 COUNTRY: United States
 DOCUMENT TYPE: Journal; Conference Article
 FILE SEGMENT: 008 Neurology and Neurosurgery
 016 Cancer
 023 Nuclear Medicine
 037 Drug Literature Index
 026 Immunology, Serology and Transplantation

LANGUAGE: English

SUMMARY LANGUAGE: English

AB Background. The ***monoclonal*** antibody anti-epidermal growth factor receptor (***EGFr***)antibody-425, against the epidermal growth factor receptor, has the potential to bind specifically to gliomas and not normal brain tissue. A prospective study was conducted (1986-1988) to evaluate the use of Indium- 111 (111In)-labeled anti- ***EGFr*** -425 in the localization of gliomas before radioimmunotherapy with Iodine-125 (125I)-labeled anti- ***EGFr*** -425. Methods. Twenty-eight patients with intracranial neoplasms were injected intravenously with an average dose of 2.2 mCi 111In-labeled anti- ***EGFr*** -425. Planar and single-photon emission computed tomography scans were performed after 48 and 72 hours. Control studies also were performed in two cases with 111In-labeled Co 17-1A (an antibody to ***colorectal*** cancer) and in one case with unlabeled 111In chloride. Results. The immunoscintigraphic findings were generally in good agreement with computerized tomographic findings. The definitive diagnosis was established by biopsy findings: 23 gliomas (1 Grade I, 5 Grade II, 6 Grade III, and 11 Grade IV), 1 meningioma, and 4 metastatic lesions. The localization of gliomas with 111In-labeled anti-EGF-425 had a sensitivity of 0.96, a specificity of 0.60 and an accuracy of 0.90. Conclusion. Immunoscintigraphy with 111-In labeled anti- ***EGFr*** -425 can be useful in the management of malignant gliomas, especially before radioimmunotherapy with 125I-labeled anti- ***EGFr*** -425.

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(FILE 'HOME' ENTERED AT 14:11:01 ON 25 OCT 2002)

FILE 'MEDLINE, EMBASE, BIOSIS, CAPLUS' ENTERED AT 14:11:12 ON 25 OCT 2002

L1 0 S OSBAND/AU
 E OSBAND/AU
 L2 248 S E4-E12
 L3 0 S IMMUNOTHERAPY/JN
 L4 0 S IMMUNOTHERAPY/JT
 L5 20 S IMMUNOTHER?/JT
 E IMMUNOTHERAPY/JT
 L6 2 S E1
 E MOLECULAR AND CELLULAR/JT
 L7 155 S E11
 E ROCKWELL/AU
 E ROCKWELL P/AU
 L8 155 S E3-E12
 L9 6 S L8 AND L7
 L10 3 DUP REM L9 (3 DUPLICATES REMOVED)
 E INTERNATIONAL JOURNAL OF ONCOLOGY/JT
 L11 10020 S E3
 L12 5 S PREWETT
 E PREWETT M/AU
 L13 92 S E3-E8
 L14 3 S L13 AND L11
 L15 1 DUP REM L14 (2 DUPLICATES REMOVED)
 L16 87104 S CANCER RESEARCH/JT
 L17 6 S AACR ANNUAL
 L18 0 S L16 AND L17
 L19 1 S IMMUNOCHEMOTHERAPY AND TRANSITIONAL AND C225

L20 14234 S EGFR OR ERBB1 OR CERBB1
 L21 674890 S MONOCLONAL OR MAB OR HUMAB RHMAB OR HUMANIZED OR CHIMERIC OR
 L22 6091 S IRINOTECAN

FILE 'REGISTRY' ENTERED AT 14:29:38 ON 25 OCT 2002
 L23 4 S IRINOTECAN

FILE 'MEDLINE, EMBASE, BIOSIS' ENTERED AT 14:30:34 ON 25 OCT 2002

FILE 'MEDLINE, EMBASE, BIOSIS, CAPLUS' ENTERED AT 14:30:42 ON 25 OCT 2002
 L24 276 S CAMPTOSAR
 L25 536 S 97682-44-5/RN
 L26 6128 S L22 OR L24 OR L25
 L27 8 S L20 AND L21 AND L26
 L28 6 DUP REM L27 (2 DUPLICATES REMOVED)
 L29 2120 S L20 AND L21
 L30 11170737 S TREAT? OR THERAP?
 L31 105236 S COLORECTAL
 L32 37 S L29 AND L30 AND L31
 L33 19 DUP REM L32 (18 DUPLICATES REMOVED)
 L34 1625 S L26 AND L30 AND L31
 L35 3066485 S GENERAL REVIEW/DT
 L36 495 S L34 AND L35
 L37 76 S L34 AND L21
 L38 57 DUP REM L37 (19 DUPLICATES REMOVED)
 L39 77 S L33 OR L38 OR L28
 L40 76 DUP REM L39 (1 DUPLICATE REMOVED)